Recent Advances in Immune Checkpoint Inhibitors in Gynaecologic & Breast Cancers

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DISCLOSURE INFORMATION

Soo Chin LEE

Grant support / Research Collaborations:
Pfizer, Eisai, Taiho, ACT Genomics, Bayer

Advisory Board / Speaker Invitation:
Pfizer, Novartis, Astra Zeneca, ACT Genomics, Eli Lilly, MSD, Roche

Conference support:
Amgen, Pfizer, Roche
# US FDA Approved Indications of Immune Checkpoint Inhibitors in Solid Tumors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approval Date</th>
<th>First Approved For</th>
<th>Other Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab (anti-CTLA4)</td>
<td>March 2011</td>
<td>Melanoma</td>
<td>RCC, Colorectal</td>
</tr>
<tr>
<td>Atezolizumab (anti-PD-L1)</td>
<td>May 2016</td>
<td>Urothelial Carcinoma</td>
<td>NSCLC, Breast (Mar 2019), Small cell lung</td>
</tr>
<tr>
<td>Avelumab (anti-PD-L1)</td>
<td>March 2017</td>
<td>Merkel Cell Carcinoma</td>
<td>Urothelial Carcinoma, Renal cell</td>
</tr>
<tr>
<td>Durvalumab (anti-PD-L1)</td>
<td>May 2017</td>
<td>Small cell lung</td>
<td></td>
</tr>
<tr>
<td>Cemiplimab-rwlc (anti-PD-1)</td>
<td>Sep 2018</td>
<td>Skin SCC</td>
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</table>

3 FDA approved IO indications in gynaecologic and breast cancers (all in the last 16 months)
<table>
<thead>
<tr>
<th>GYNAECOLOGIC CANCERS</th>
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</thead>
<tbody>
<tr>
<td><strong>Cervix</strong></td>
</tr>
<tr>
<td>Single agent pembrolizumab</td>
</tr>
<tr>
<td>- <em>US FDA approval in June 2018</em></td>
</tr>
<tr>
<td>- KEYNOTE 158; previously treated, PD-L1+</td>
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<table>
<thead>
<tr>
<th><strong>Endometrial</strong></th>
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<tbody>
<tr>
<td>Single agent pembrolizumab</td>
</tr>
<tr>
<td>- <em>US FDA approval in May 2017</em></td>
</tr>
<tr>
<td>- Le et al; mismatch repair deficient tumors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pembrolizumab + lenvatinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>- <em>US FDA approved in May 2019</em></td>
</tr>
<tr>
<td>- Makker et al; MSS tumors</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>Ovarian</strong></th>
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</thead>
<tbody>
<tr>
<td>Two negative phase III randomized trials</td>
</tr>
<tr>
<td>Avelumab + chemotherapy</td>
</tr>
<tr>
<td>- JAVELIN 200 (previously treated)</td>
</tr>
<tr>
<td>- JAVELIN 100 (first-line)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>BREAST CANCERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triple Negative, Metastatic First-line</strong></td>
</tr>
<tr>
<td>Atezolizumab + chemotherapy</td>
</tr>
<tr>
<td>- <em>US FDA approval in March 2019</em></td>
</tr>
<tr>
<td>- IMPASSION 130, PD-L1+ (SP142, ≥1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Triple Negative, Neoadjuvant</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab + chemotherapy</td>
</tr>
<tr>
<td>- Keynote 522, ESMO 2019</td>
</tr>
<tr>
<td>- Increased pCR, promising EFS signal</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Triple Negative, Previously Treated</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Single agent pembrolizumab</td>
</tr>
<tr>
<td>- KEYNOTE 119, ESMO 2019</td>
</tr>
<tr>
<td>- Negative for ITT; promising signal in high PD-L1 (22C3, CPS≥20) tumors</td>
</tr>
</tbody>
</table>
Immune Checkpoint Inhibitors in Gynaecologic Cancers
Rationale of Immune Checkpoint Inhibitors in Gynaecologic Cancers

High PD-L1 expression in gynaecologic cancers
- Epithelial ovarian ~65%, endometrial ~75%, cervix ~65%

**Cervix Cancer**
- Largely related to HPV (immunologically foreign antigens for immune system to target)

**Endometrial Cancer**
- Subset of MSI-high/dMMR tumors

**Epithelial Ovarian Cancer**
- High prevalence of tumor infiltrating lymphocytes (~50%)  
- A subset of patients has high neoantigen load  
- Uses PD-L1 pathway as tumor resistance mechanism
Development Strategies of Immune Checkpoint Inhibitors in Gynaecologic Cancers

Single agent Immune Checkpoint Inhibitors

**Combinations**
- With *chemotherapy*
- With *other Immune Checkpoint Inhibitor(s)*
- With *targeted agents*
  - With anti-angiogenic agents *(immune suppressive activity of VEGF)*
  - With PARP inhibitors *(PARPi cause DNA damage, providing tumor neoantigens)*
**Immune Checkpoint Inhibitors in Cervix Cancer**

**Pembrolizumab**

**KEYNOTE 158 (Basket trial; single arm)** *(Chung et al, JCO 2019)*

N=98 previously treated cervix cancer, **83.7% PD-L1 positive (CPS ≥1)**

i/v pembrolizumab 200mg, 3 weekly

**ORR 12.2% (all in PD-L1 positive tumors)**; 3% CR, 9% PR

Median duration of response not reached (median FU 10.2 months) (range, ≥3.7 to ≥18.6 months)

*June 2018:* US FDA approved *pembrolizumab* for **recurrent or metastatic cervical cancer** with *disease progression on or after chemotherapy* whose tumors express **PD-L1 (CPS ≥1)** as determined by an FDA-approved test

**METASTATIC 1ST LINE PEMBROLIZUMAB:** KEYNOTE 826 (Phase III Randomized)

Target: n=600 recurrent/metastatic cervix cancer; Started Oct 2018 *(NCT03635567)*

**Unselected for PD-L1;** Primary endpoints: PFS, OS

<table>
<thead>
<tr>
<th>R1:1</th>
<th>Paclitaxel + Cisplatin or Carboplatin +/- Bevacizumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paclitaxel + Cisplatin or Carboplatin +/- Bevacizumab</td>
<td>Pembrolizumab 200mg, 3 weekly</td>
</tr>
</tbody>
</table>
**2012:** observation that a patient who responded very well to immune checkpoint inhibitor (nivolumab) has Lynch syndrome

**Phase II trial**
- N=86 patients, 12 different tumor types, **17 endometrial cancers**
- Tumor showed **mismatch repair defect** (MSI, IHC)
- 37% had **germline MLH1/MSH2/MSH6 mutations** (Lynch syndrome)
- Progressed on at least one prior therapy
- Treated with **pembrolizumab**

**Median PFS not reached (median FU 12.5 mths)**

**Estimated PFS:** 1Y 64%, 2Y 53%

**CR 21%, PR 32%**

**Biomarker:** Microsatellite instability or dMMR (IHC)

**Drug:** Pembrolizumab

Agnostic biomarker (any solid tumor)

**N=7725 unselected endometrial tumors** tested from 23 studies

**25%** (range 7-36%) demonstrate **MSI or mismatch repair defect** on IHC

Ryan et al. Genetics in Medicine, May 2019

Topolian et al. NEJM, 2012; 366: 2443-54; Le et al. Science 2017
**Immune Checkpoint Inhibitors in Endometrial Cancer**

**Pembrolizumab + Lenvatinib (RET + VEGF-R TKI)**

**Study 111/KEYNOTE 146** *(Makker et al. Lancet Oncol 2019; 20(5): 711-8)*

Single arm phase II trial
N=108 metastatic endometrial carcinoma; ≤2 prior systemic therapies

87% non-MSI-H/dMMR

i/v pembrolizumab 200mg, 3 weekly + PO lenvatinib 20mg daily

**ORR 38.3%** in non-MSI-H/dMMR tumors (CR 10.6%, PR 27.7%)

69% of responders had **duration of response ≥6 months**

**September 2019:** US FDA approved pembrolizumab + lenvatinib for **advanced endometrial carcinoma** who have **disease progression following prior systemic therapy** and that is **NOT MSI-H or mismatch repair deficient**

**METASTATIC 2nd LINE PEMBROLIZUMAB:** KEYNOTE 775 (Phase III Randomized)

Started June 2018 *(NCT03517449); ONGOING*

Target: n=780 advanced endometrial cancer (120 MMR deficient, 660 MMR proficient)

**Progressed after 1 prior platinum-based therapy; stratify by MMR status**

- Pembrolizumab + Lenvatinib
- Physician’s choice chemotherapy (doxorubicin or paclitaxel)
# Immune Checkpoint Inhibitors in Ovarian Cancer

## Avelumab + Chemotherapy (Negative Randomized Trials)

### METASTATIC REFRACTORY, AVELUMAB: JAVELIN 200 (Phase III Randomized)
- n=566 platinum-resistant or refractory epithelial ovarian cancer
- (13% clear cell, 25% platinum refractory)
- ≤3 prior lines of therapy; 57% PD-L1+

<table>
<thead>
<tr>
<th>Arm</th>
<th>Avelumab alone</th>
<th>Liposomal doxorubicin</th>
<th>Avelumab + Liposomal doxorubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td>1.9</td>
<td>3.5</td>
<td>3.7</td>
</tr>
<tr>
<td>OS</td>
<td></td>
<td>13.1</td>
<td>15.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PD-L1+ (mths)</th>
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</thead>
<tbody>
<tr>
<td>PFS OS</td>
</tr>
<tr>
<td>3.0 13.1</td>
</tr>
<tr>
<td>(HR 0.65)</td>
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<tr>
<td>17.7 (HR 0.72)</td>
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<tr>
<td>(0.46-0.92)</td>
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<tr>
<td>(0.48-1.08)</td>
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</tbody>
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R 1:1:1

### METASTATIC FIRST-LINE, AVELUMAB: JAVELIN 100 (Phase III Randomized)
- n= 998 stage III-IV Epithelial Ovarian, fallopian tube or primary peritoneal cancer
- Unselected for PD-L1

<table>
<thead>
<tr>
<th>Arm</th>
<th>Carboplatin + Paclitaxel</th>
<th>Maintenance Avelumab + TALAZOPARIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td>3.0 (HR 0.65)</td>
<td></td>
</tr>
<tr>
<td>OS</td>
<td>13.1 (HR 0.72)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.46-0.92)</td>
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<tr>
<td></td>
<td>(0.48-1.08)</td>
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</tbody>
</table>

R 1:1:1

### METASTATIC FIRST-LINE, AVELUMAB: JAVELIN 100 PARP (Phase III Randomized)
- Stage III-IV locally advanced/metastatic ovarian cancer
- Unselected for PD-L1

- Terminated early in Jan 2019 (unlikely to achieve PFS benefit)

R

<table>
<thead>
<tr>
<th>Arm</th>
<th>Avelumab + Carboplatin + Paclitaxel</th>
<th>Maintenance Avelumab + TALAZOPARIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OS</td>
<td></td>
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</tbody>
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R 1:1:1

**Overall Negative Trial**

Too many poor prognostic patients?
Immune Checkpoint Inhibitors in Breast Cancer
Among Breast Cancer Subtypes, TNBC is more likely to respond to Immune Checkpoint Inhibitors

TNBCs have high tumor mutational burden among breast cancer subtypes

Tumor infiltrating lymphocytes are common in TNBC and are prognostic

PD-L1 expression higher in HR- versus HR+ breast cancers

TNBC have generally poor prognosis with limited treatment options (unmet clinical need)

Gianni et al. SABCS 2016
Loi et al. JCO 2013, 31(7): 860-7;
Kim et al. BMC Cancer 2017; 17(1): 690
Immune Checkpoint Inhibitors in Breast Cancer

Current Developmental Status

Clinical trials.gov
- >120 trials that allow inclusion of breast cancer patients
- >70 trials that are exclusive to breast cancer

Triple Negative Breast Cancer
- HER2+
- Hormone receptor positive

Atezolizumab
- Pembrolizumab
- Avelumab
- Nivolumab
- Durvalumab
- Others
Atezolizumab in TNBC: Early Phase Data

**Single agent atezolizumab**
- 1200mg every 3 weeks
- N=116 metastatic TNBC (Phase I)

**Median duration of response** 21 months

**ORR by subgroup**
- 1L vs ≥2L: 24% vs 6%
- PD-L1+ vs neg: 12% vs 0%

**Atezolizumab + Chemotherapy**
- Atezolizumab (800mg, 2-weekly)
- Nab-paclitaxel (125mg/m², D1, 8, 15, q28 days)
- N=33 metastatic TNBC (Phase Ib)

**Median duration of response** 21 months

**ORR by subgroup**
- 1L vs ≥2L: 58% vs 30%
- PD-L1+ (>1%) vs PD-L1-: 41% vs 33%

**Key observations:**
- ORR higher:
  - 1L vs ≥2L
  - PD-L1+ vs PD-L1-
  - with chemo vs single agent
- Durable response and long survival in some patients

Schmid et al. AACR 2017; Emens et al. JAMA Onc Sep 2018; Adams et al. JAMA Onc Oct 2018
Atezolizumab + Chemotherapy in TNBC: IMPassion 130

**METASTATIC FIRST-LINE ATEZOLIZUMAB; IMPASSION 130 (Phase III Randomized)**

n= 902 metastatic TNBC; **Unselected for PD-L1**

41% PD-L1 positive (SP142, ≥1%)

- Nab-paclitaxel 100mg/m², D1, 8, 15, Q4W
- Placebo
- Nab-paclitaxel 100mg/m², D1, 8, 15, Q4W
- Atezolizumab 840mg Q2W

**Primary endpoint:** PFS and OS (ITT, PD-L1+ group)

- **ITT (n=902)**
  - 5.5 vs 7.2, \(\Delta 1.7\) months
  - HR 0.80, p=0.0025

- **PD-L1+ (n=369)**
  - 5.0 vs 7.5, \(\Delta 2.5\) months
  - HR 0.62, p<0.001

**US FDA approved atezolizumab in first-line treatment of PD-L1+ metastatic TNBC (SP142) in March 2019**

**Schmid et al. NEJM Oct 2018**
# Atezolizumab in TNBC: Ongoing Phase III Randomized Trials

## Metastatic 1st Line Atezolizumab

**IMPASSION 131 (Phase III Randomized)**  
Target: n= 540 metastatic TNBC  
Started August 2017 (*NCT03125902*)  
Unselected for PD-L1

<table>
<thead>
<tr>
<th>Arm</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>Paclitaxel 90mg/m², D1, 8, 15, Q4W</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td>R</td>
<td>Paclitaxel 90mg/m², D1, 8, 15, Q4W</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab 840mg, Q2W</td>
</tr>
</tbody>
</table>

**IMPASSION 132 (Phase III Randomized)**  
Target: n= 350 metastatic TNBC  
Started Jan 2018 (*NCT03371017*)  
Unselected for PD-L1

<table>
<thead>
<tr>
<th>Arm</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>Gemcitabine + Carboplatin OR Capecitabine</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td>R</td>
<td>Gemcitabine + Carboplatin OR Capecitabine</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab 1200mg, Q3W</td>
</tr>
</tbody>
</table>

## Adjuvant Atezolizumab: IMPASSION 030 (Phase III Randomized)

Started August 2018 (*NCT03498716*); Unselected for PD-L1  
Target: n= 2300 stage II-III TNBC (50% node positive)

<table>
<thead>
<tr>
<th>Arm</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/R</td>
<td>Paclitaxel weekly x 12, ddAC/EC x 4</td>
</tr>
<tr>
<td>S/R</td>
<td>Paclitaxel weekly x 12, ddAC/EC x 4</td>
</tr>
<tr>
<td>S/R</td>
<td>Atezolizumab 840mg Q2W x 10 doses cycles, then 1200mg Q3W to complete 1 year</td>
</tr>
</tbody>
</table>

Several ongoing phase II/III randomized **neoadjuvant atezolizumab + chemotherapy trials** *(NeoTRIPaPDL1, IMPassion 031, NSABP-B59/GeparDouze)*
Neoadjuvant Pembrolizumab + Chemotherapy in TNBC

**NEOADJUVANT PEMBROLIZUMAB**: I-SPY2 (Phase II Adaptive Randomized Design)

- N=180 HER2-
  - Paclitaxel x 12 weeks
  - AC x 4 (60/600) [pCR in TNBC: 20% (13% for HR+/HER2-)]

- N=69 HER2- (n=29 TNBC)
  - Paclitaxel x 12 weeks
  - AC x 4 (60/600) [pCR in TNBC: 60% (34% for HR+/HER2-)]

>99% predicted probability of phase III success in TNBC
88% predicted probability of phase III success in HR+, HER2- breast cancer

**NEOADJUVANT PEMBROLIZUMAB**: KEYNOTE 522 (Phase III Randomized)

- n= 602 TNBC; Unselected for PD-L1
- Co-primary end-points: pCR, EFS
- Carboplatin added to the neoadjuvant regimen
- Pembrolizumab combined with neoadjuvant EC/AC Adjuvant Pembrolizumab

- Paclitaxel/Carboplatin x 12 weeks
  - EC/AC x 4
  - Placebo

- Paclitaxel/Carboplatin x 12 weeks
  - EC/AC x 4
  - Pembrolizumab 3 weekly x 8

- Placebo 3 weekly x 9

Nanda, Proc ASCO 2017; Schmid et al. ESMO 2019
Neoadjuvant Pembrolizumab + Chemotherapy in TNBC

Keynote 522

PD-L1+ tumors more likely to achieve pCR (with or without pembrolizumab). PD-L1 expression did not select for patients who benefit from pembrolizumab.

Primary Endpoint: ypT0/Tis ypN0

pCR; ITT (n=602)

By PD-L1 Status: ypT0/Tis ypN0

PD-L1+ (n=498)  PD-L1- (n=97)

By PD-L1 Status: ypT0/Tis ypN0

By PD-L1 Status: ypT0/Tis ypN0

Event-Free Survival at IA2

Δ 6% at 18 months

EFS HR 0.63 (0.43-0.93)

Schmid et al. ESMO 2019
Single Agent Pembrolizumab in Previously Treated TNBC

**METASTATIC 2\textsuperscript{nd}/3\textsuperscript{rd} LINE PEMBROLIZUMAB:** KEYNOTE 119 (Phase III Randomized)  
Target: n= 600 metastatic TNBC; Started Oct 2015 (NCT02555657); Unselected for PD-L1  
Primary endpoints: OS (ITT, CPS ≥1, CPS ≥10)

Physician’s choice single agent chemotherapy  
*Capecitabine, eribulin, vinorelbine, or gemcitabine*  
Pembrolizumab 200mg, 3 weekly x up to 35 cycles

**Overall negative trial**  
High CPS score (≥20) may select patients who benefit

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**Overall Survival by PD-L1 CPS**

<table>
<thead>
<tr>
<th>CPS ≥1</th>
<th>~65% of population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>85.3%</td>
<td>0.97 (0.82-1.15)</td>
</tr>
<tr>
<td>88.1%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CPS ≥10</th>
<th>~30% of population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>77.4%</td>
<td>0.78 (0.57-1.06)</td>
</tr>
<tr>
<td>88.8%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>CPS ≥20</th>
<th>~18% of population (Exploratory Analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>HR (95% CI)</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>70.2%</td>
<td>0.58 (0.38-0.88)</td>
</tr>
<tr>
<td>92.3%</td>
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Cortes KN119 ESMO 2019
Immune Checkpoint Inhibitors in Non-Triple Negative Breast Cancers

**HR+, HER2-, PD-L1+ MBC**
- N=25 patients; PD-L1+ (CPS≥1)
- Median no. of prior therapies 9 (3-15)
- Single agent pembrolizumab 10mg/kg Q2W
- ORR 12%, SD 16%
- Median duration of response 12 months
- 19.4% of evaluable HR+/HER2 MBC were PD-L1+

**HER2+ MBC** (PANACEA; Phase Ib/II)
- N=52 (40 PD-L1+, 12 PD-L1-; [CPS≥1])
- Progressed on prior trastuzumab-based therapies
- Pembrolizumab 200mg Q3W + Trastuzumab

<table>
<thead>
<tr>
<th></th>
<th>ORR</th>
<th>12-mth PFS</th>
<th>12-mth OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 positive (n=40)</td>
<td>15%</td>
<td>13%</td>
<td>65%</td>
</tr>
<tr>
<td>PD-L1 negative (n=12)</td>
<td>0%</td>
<td>0%</td>
<td>12%</td>
</tr>
</tbody>
</table>

Promising efficacy signal in PD-L1+ non-TNBC

1 patient with sustained PR for 32.3 months

# Immune Checkpoint Inhibitors in Gynaecologic and Breast Cancers: Summary

## PREVIOUSLY TREATED CERVIX CARCINOMA

<table>
<thead>
<tr>
<th>PD-L1+ with CPS (~60-70%)</th>
<th>PD-L1-</th>
</tr>
</thead>
</table>

- Single agent pembrolizumab *(Keynote 158; ORR 12%, durable response)*
  - (FDA approved)

## PREVIOUSLY TREATED ENDOMETRIAL CARCINOMA

<table>
<thead>
<tr>
<th>MSI-H/dMMR (~25%)</th>
<th>Non-MSI-H/dMMR (~75%)</th>
</tr>
</thead>
</table>

- Single agent pembrolizumab *(FDA approved)*
  - *(Le et al. 50-60% ORR, durable response)*
- Pembrolizumab + Lenvatinib *(FDA approved)*
  - *(Makker et al. 40% ORR, durable response)*

## EPITHELIAL OVARIAN CANCER

Currently no data to support use of Immune Checkpoint Inhibitors *(2 negative Phase III Randomized Trials)*

## TRIPLE NEGATIVE BREAST CANCER

- **Clinical Stage II-III (Neoadjuvant)**
  - Pembrolizumab + (carboplatin/paclitaxel → AC/EC)
    - *(Positive Phase III Randomized data)*
    - *(KEYNOTE 522, pCR ↑15%, EFS HR 0.63)*

- **Metastatic First-line**
  - PD-L1+ (~ 40%)
    - With SP142
  - PD-L1-
    - Atezolizumab + Nab-paclitaxel *(FDA approved)*
      - *(IMPASSION 130, OS benefit)*
Immune Checkpoint Inhibitors in Gynaecologic and Breast Cancers: Conclusions

Early Stage Disease | Metastatic 1st line | Metastatic 2nd line and beyond

BREAST | IO? TNBC | IO TNBC
CERVIX |  | IO PD-L1+
ENDOMETRIAL | IO MSI+ | IO MSI-
OVARY

Small but significant progress made in the last 18 months
Still many opportunities for further development

Continue Enrolling into the many ongoing trials!