
# Immunotherapy and new drugs in advanced cervical cancer

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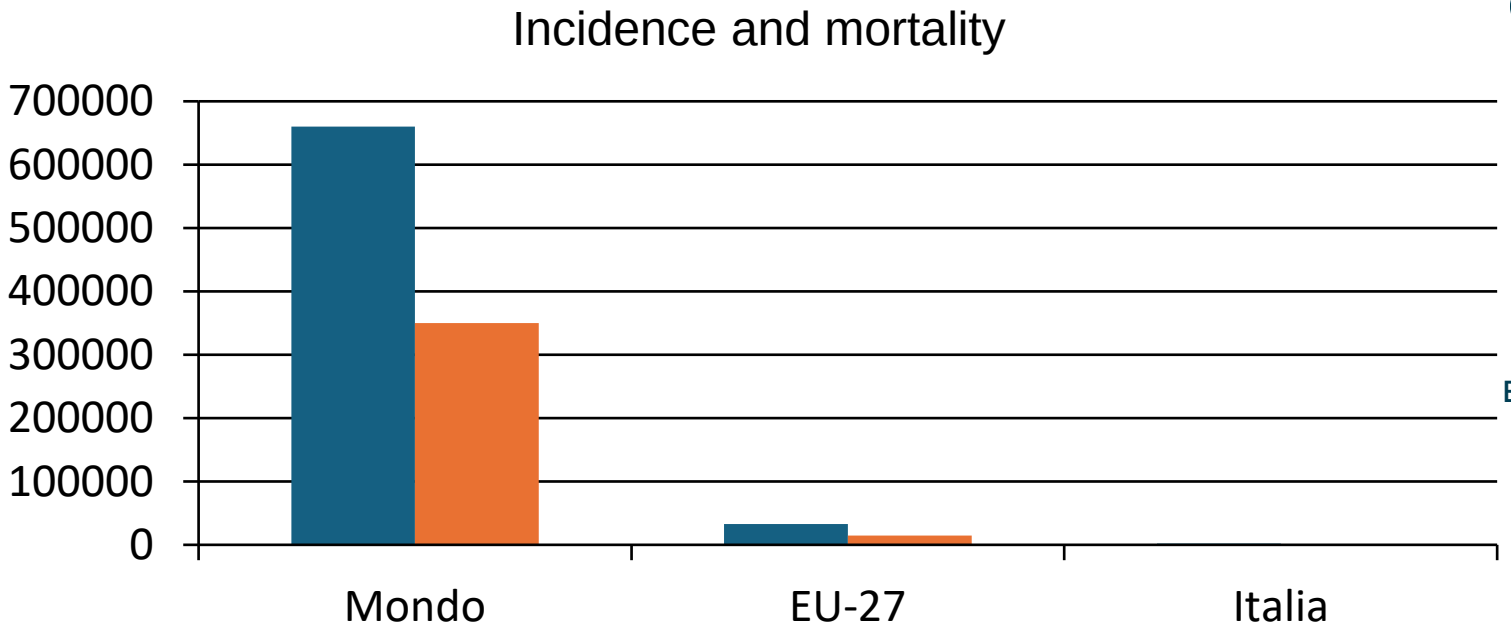
# Cervical cancer tumour burden




Global (GLOBOCAN 2024)

660,000 new cases/y

350,000 deaths/y,

**with 90% occurring in low- and middle-income countries**

EU Europe (EURACAN – EU-27)

~33,000 new cases/y

7.6 cases per 100,000 women/y

IT Italy (AIOM–AIRTUM 2024)

~2,400 new cases/y

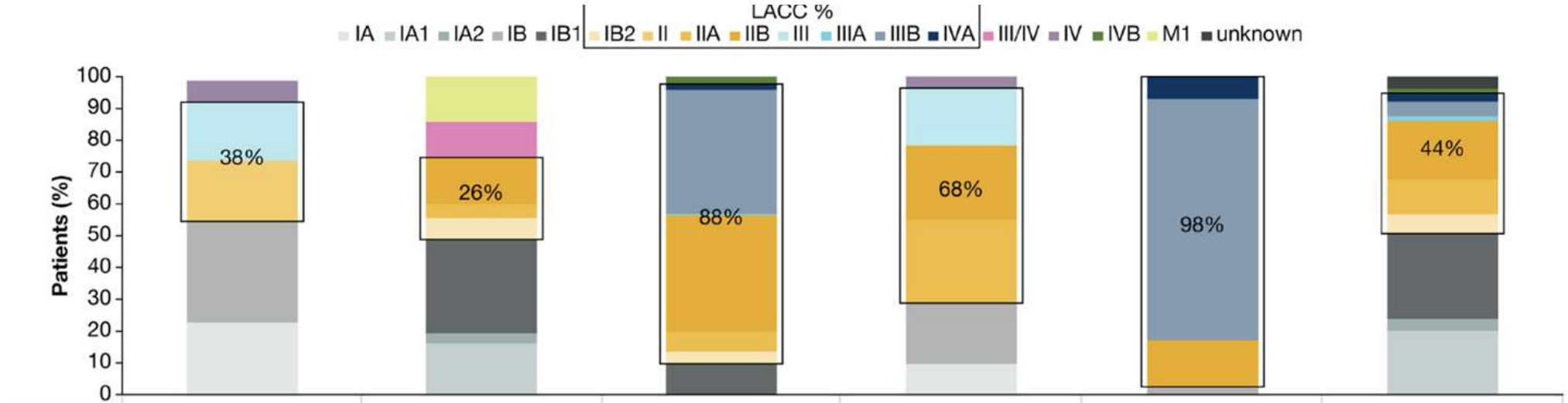
~1,000 deaths/y

**Incidence is decreasing thanks to:**

- **HPV vaccination**
- **Cervical cancer screening programs (Pap smear and HPV DNA test)**

*Sung H et al., CA Cancer J Clin, 2024,*
*EURACAN, 2024,*
*AIRTUM, 2024*

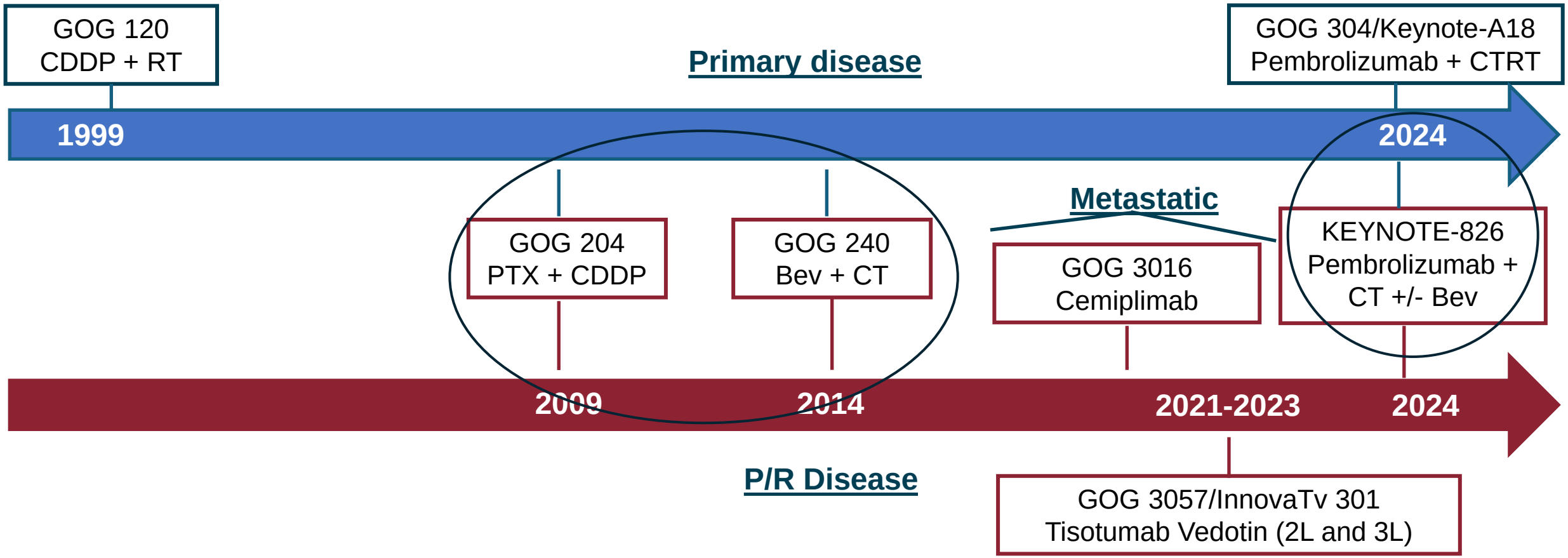
# Proportions and incidence of locally advanced cervical cancer: a global systematic literature review




| Reference | Mahmud 2011 | Rottmann 2020 | Elmajjaoui 2016 | Kaidarova 2018 | Shruthi 2014 | Seol 2014 |
|---|---|---|---|---|---|---|
| N (All cervical cancer) | 714 | 2291 | 646 | 1641 | 199 | 19 282 |
| Location | Canada Saskatchewan | Germany Upper Bavaria | Morocco | Kazakhstan | India Kolar | Korea |
| Data collection period | 1987-2001 | 2007-2016 | 2006 | 2012 | 1-year period (date not reported) | 1999-2004 |
| | North America | Europe | Africa | Asia | | |

*Monk BJ, et al. Int J Gynecol Cancer 2022*

# Practice changing trials

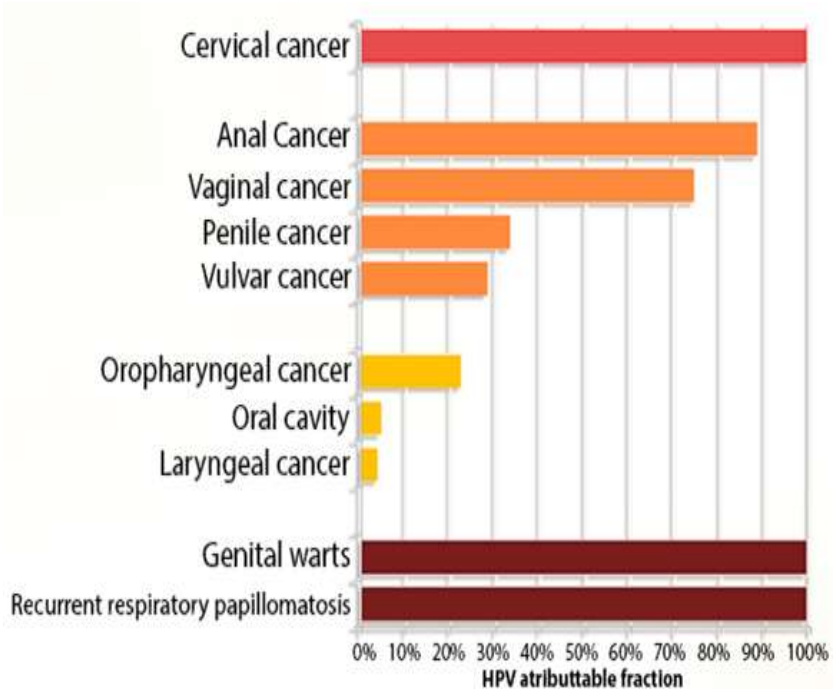



*1. Rose PG et al. N Engl J Med. 1999;340:1144-1153. 2. Monk BJ et al. J Clin Oncol. 2009:27:4649-4655. 3. Tewari KS et al. N Engl J Med. 2014;370:734-743. 4. Tewari KS et al. Lancet. 2017:390:1654-1663. 5. Colombo N et al. N Engl J Med. 2021:385:1856-1867. 6. Monk BJ et al. J Clin Oncol. 2023;41:5505-5511. 7. Vergote I et al. N Engl J Med. 2024;391:44-55. 8. Lorusso D et al. Lancet. 2024:403:1341-1350. 9. Tewari KS, Monk BJ. N Engl J Med. 2022,386:544-555.*


with **IMMUNOTHERAPY**

# Rationale for immunotherapy (CC is a HPV related tumor)

| | Type of cancer | HPV | | HPV positive % |
|---|---|---|---|---|
| | cervical | 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 | | >95 |
| vulvar | basaloid | 16, 18 | | >50 |
| | warty | 16, 18 | | >50 |
| | keratinising | 16 | | <10 |
| penile | basaloid | 16, 18 | >50 | |
| | warty | 16, 18 | >50 | |
| | keratinisng | 16 | <10 | |
| | vaginal | 16, 18 | >50 | |
| | anal | 16, 18 | >70 | |
| | Oral cavity | 16, 18, 33 | | 25 |

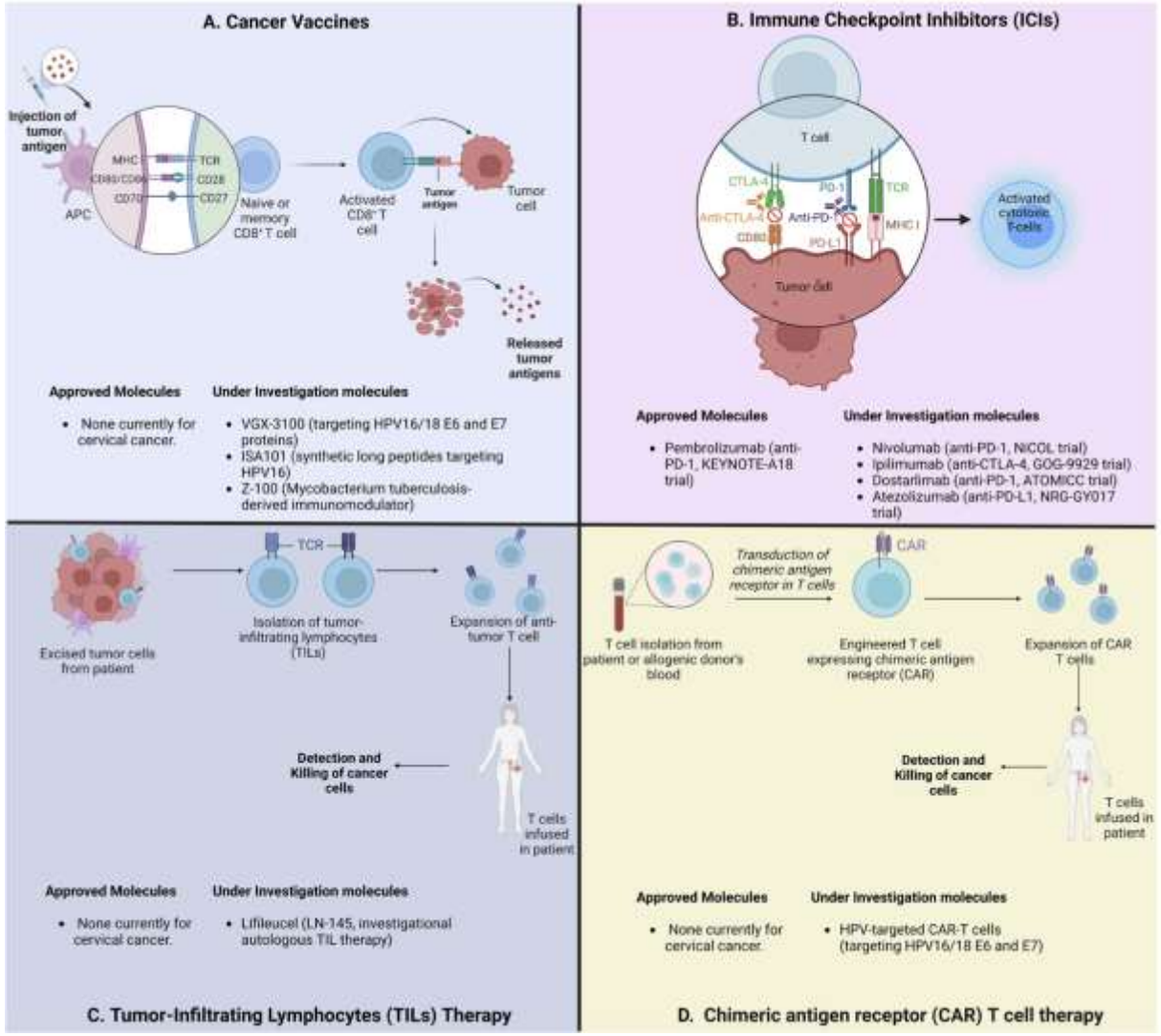



## CANCER HISTOLOGY HPV BASED

- ✔ 65-70% of adenocarcinomas are HPV related
- ✔ 85-90% of squamous cervical cancer are HPV related

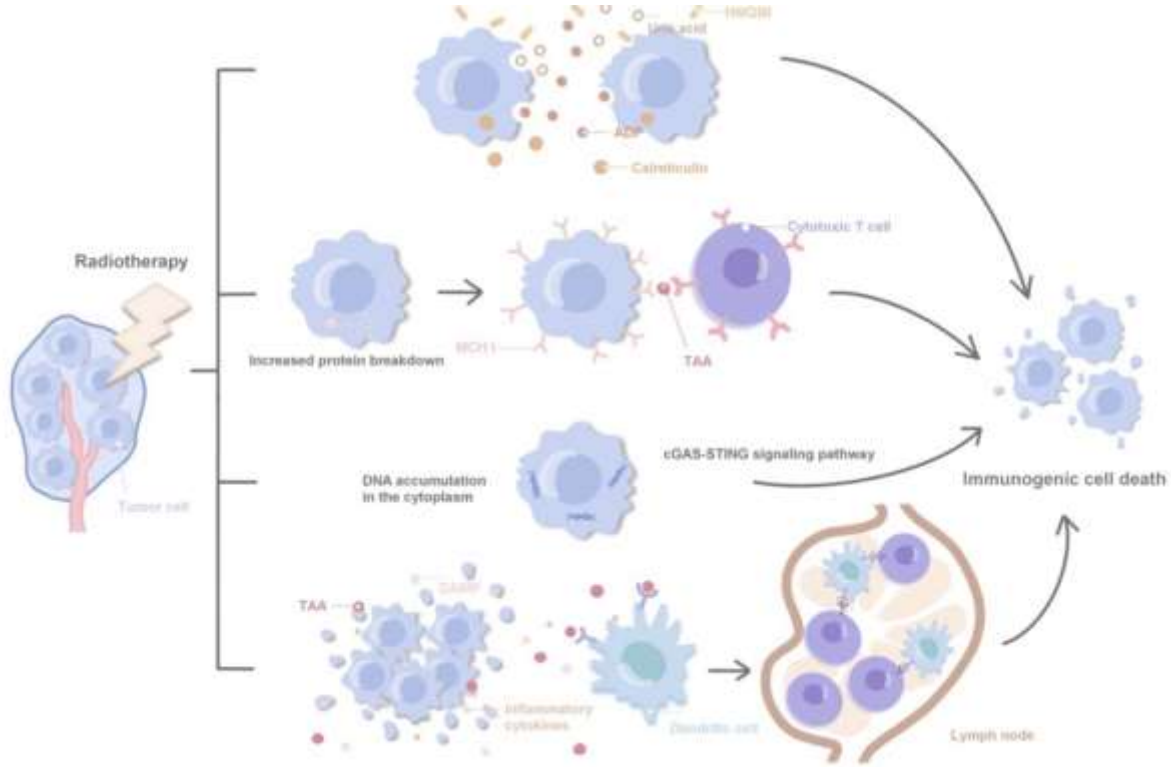
*Chong GO et al., Gynecol Oncol 2017*

# Rationale for immunotherapy




PDL1 expression

- CPS≧1 89%
- CPS≧10 ~50%




*Colombo N et al., NEJM 2021; Yang X et al., J Cancer 2022*

# Practice changing trials of immunotherapy



| ICI | Trial | Author, Year | Line / Setting | PFS (mo) | OS (mo) | Approval (FDA,EMA,AIFA) |
|---|---|---|---|---|---|---|
| **Pembrolizumab (monotherapy)** | KEYNOTE-158 (Phase II) | Marabelle A et al., Nat Cancer. 2025 | 2nd-line recurrent/metastatic, PD-L1 (CPS ≥1) | mPFS ~ 4 mo | ORR ~ 33.8%, mOS ~19.8 mo | ☑ FDA ✗ EMA, ✗ AIFA |
| **Pembrolizumab + CT ± Bev** | KEYNOTE-826 (Phase III) | Monk BJ et al., J Clin Oncol. 2023 | 1st-line persistent/recurrent/metastatic, CPS ≥1 | 10.5 vs 8.2 (HR 0.62) | 28.6 vs 16.5 (HR 0.60) | ☑ FDA ☑ EMA ☑ AIFA |
| **Pembrolizumab + CRT** | KEYNOTE-A18 (Phase III) | Lorusso D et al., Lancet 2024 | 1st-line high-risk locally advanced (FIGO III–IVA) | NR; 24-mo PFS 68% vs 57% (HR 0.70) | NR; 36-mo OS 82.6% vs 74.8% (HR 0.67) | ☑ FDA ✗ EMA, ✗ AIFA |
| **Cemiplimab (monotherapy)** | EMPOWER-Cervical-1 (Phase III) | Oaknin A et al., Eur J Cancer. 2025 | 2nd-line recurrent/metastatic | 2.8 vs 2.9 (HR 0.75) | 11.7 vs 8.5 (HR 0.67) | ☑ FDA ☑ EMA ☑ AIFA |

# What about extra US and UE countries?


| Drug (Generic Name) | Mechanism | Country/Region | Approved Indication | Approval Year | Key Notes |
|---|---|---|---|---|---|
| **Pembrolizumab (Keytruda)** | Anti–PD-1 monoclonal antibody | USA; Asia (trials) | PD-L1+ R/M cervical cancer + and after platinum chemo; +CCRT for LACC (based on trial data) | USA: 2021 (R/M); 2024 (LACC) | KEYNOTE-A18 showed benefit in Asian subgroup (PFS HR ~0.55) |
| **Zimberelimab (YuTuo®)** | Anti–PD-1 monoclonal antibody | China (NMPA) | PD-L1+ recurrent/metastatic cervical cancer after platinum chemotherapy | 2023 | First approved ICI for cervical cancer in China; ORR ~27.8% in Phase II study |
| **Cadonilimab (AK104)** | Bispecific anti–PD-1/CTLA-4 | China | Recurrent/metastatic cervical cancer after platinum chemotherapy | 2022 | First bispecific ICI approved for cervical cancer worldwide |
| **Tislelizumab** | Anti–PD-1 monoclonal antibody | China | Investigational (+CCRT in locally advanced cervical cancer) | Not yet approved | Phase II Chinese trial shows promising ORR (100% interim CR+PR) |

# EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9 study design (NCT03257267) Final OS

Rec and metastatic CC after platinum-based CT

Regardless PDL1 status

Cemiplimab 350 mg Q3W IV

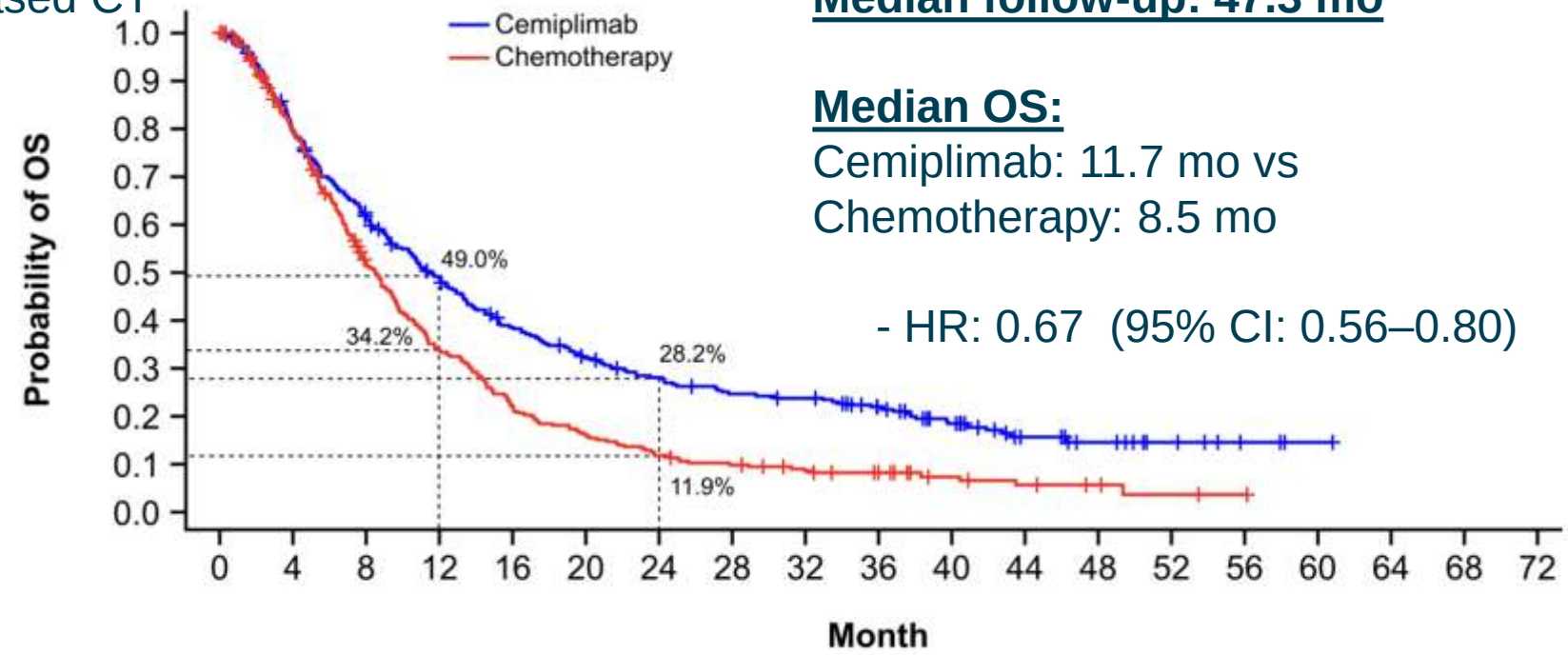
IC chemotherapy

**Options:**

- Pemetrexed 500 mg/m² Q3W IV
- Gemcitabine 1,000 mg/m² IV on Days 1 and 8 and every 21 days
- Topotecan 1 mg/m² daily IV for 5 days, every 21 days
- Irinotecan 100 mg/m² IV weekly x 4, followed by 10–14 days rest
- Vinorelbine 30 mg/m² IV on Days 1 and 8 and every 21 days

Stratification:

- Histology,
- Geographic region,
- Prior Bevacizumab,
- ECOG PS




**Median follow-up: 47.3 mo**

**Median OS:**

Cemiplimab: 11.7 mo vs

Chemotherapy: 8.5 mo

- HR: 0.67 (95% CI: 0.56–0.80)

| PD-L1 Status | Cemiplimab n | Cemiplimab OS (mo) | Chemo n | Chemo OS (mo) | HR (95% CI) |
|---|---|---|---|---|---|
| ≥1% | 82 | 13.9 (9.6–17.4) | 80 | 9.3 (7.0–11.4) | 0.72 (0.50–1.02) |
| <1% | 44 | 8.2 (4.3–12.3) | 48 | 6.7 (3.9–11.8) | 0.86 (0.54–1.37) |

SCC HR 0.698 (0.570-0.855)

Non-SCC HR 0.552 (0.372-0.819)

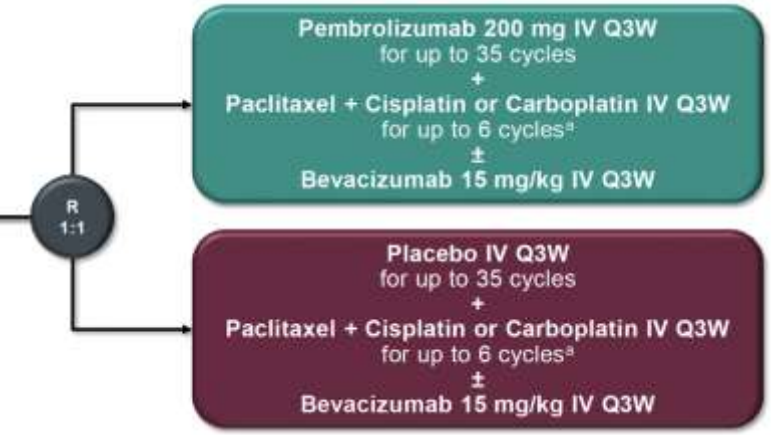
*Oaknin A. et al., EJC 2024*

# KEYNOTE-826 Protocol-specified final OS

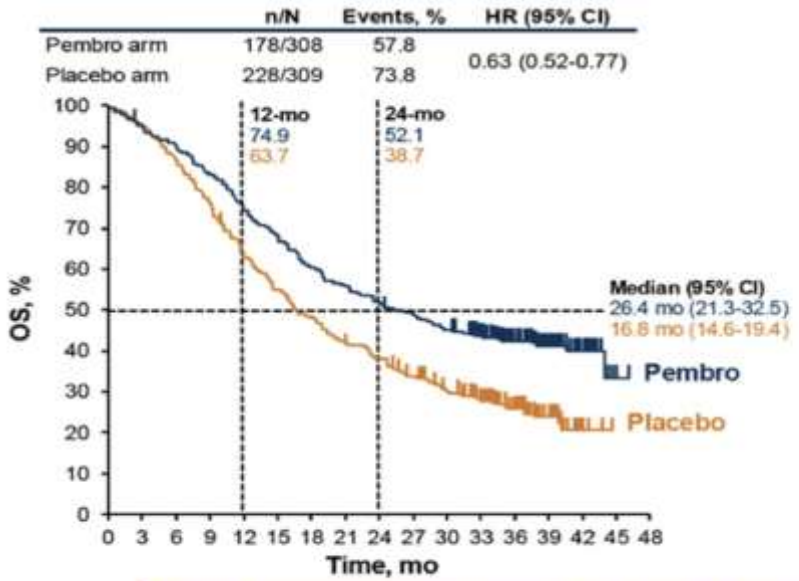
Key Eligibility Criteria

- P/R or metastatic CC not amenable to curative treatment
- No prior systemic chemotherapy (prior RT and CTRT were permitted)
- ECOG PS 0 or 1

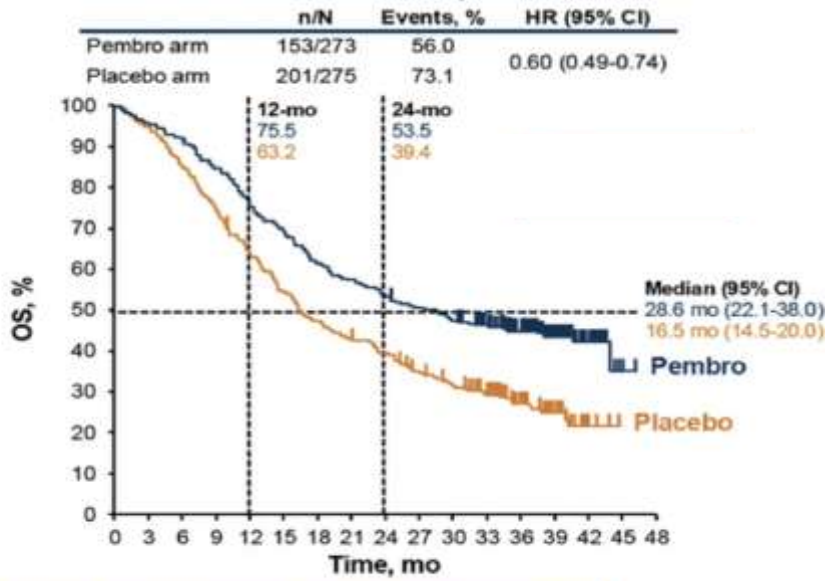
**617 pts**




**All comers**




**PDL1 CPS ≧ 1**



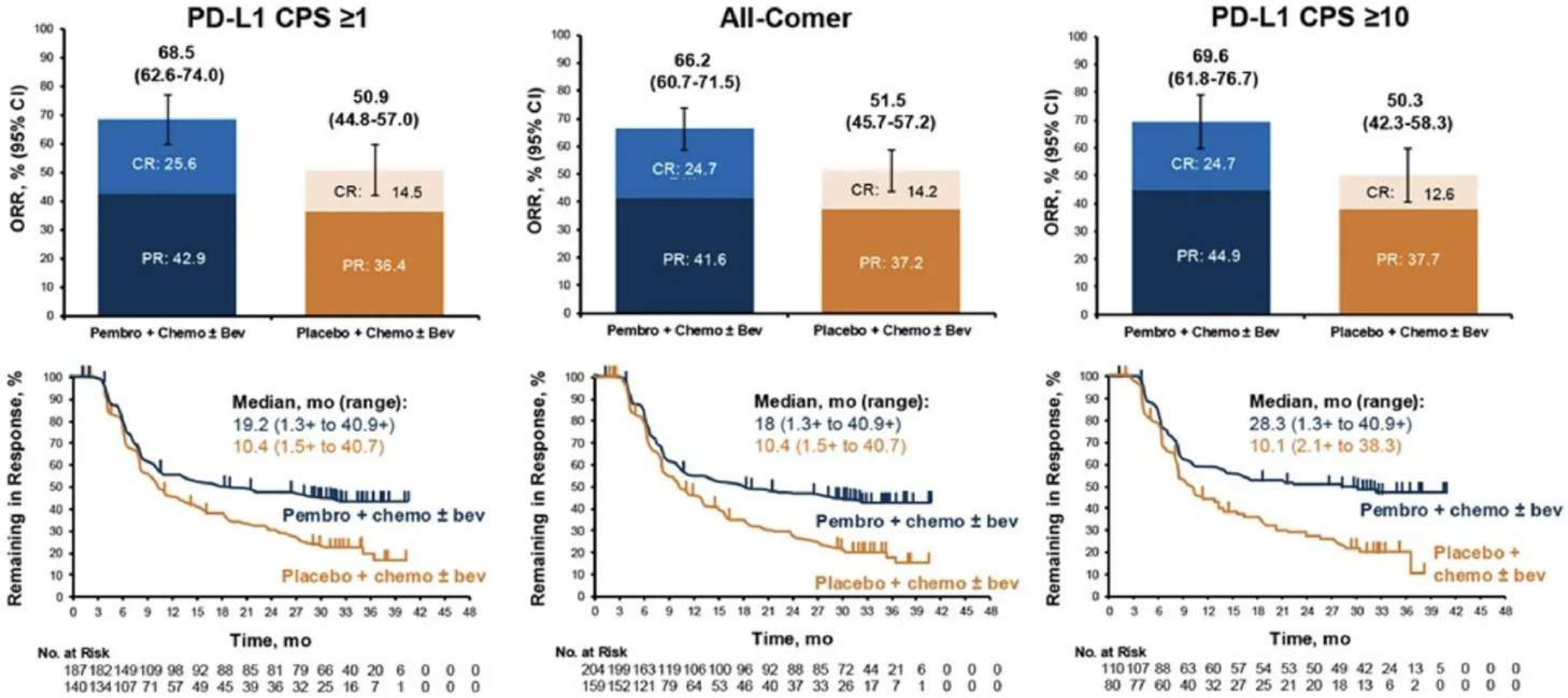

QOL was also not negatively affected with the combination of pembrolizumab plus chemotherapy[2]

Stratification:

- Metastatic disease at diagnosis (yes vs no)
- PD49 OPD (08 SE 8 80 940 00 990)
- Planned bevacizumab use (yes vs no)

*Colombo N et al., NEJM 2021*

# KEYNOTE-826 Final ORR and DOR




*Colombo N et al., NEJM 2021*

# Why is the approval for CPS ≧ 1?

**KEYNOTE-826 had a hierarchical testing strategy design.**

The primary endpoints were tested sequentially across pre-specified subgroups in the following order:
1. PD-L1 CPS ≥1 population
2. All-comers (intent-to-treat population)
3. PD-L1 CPS ≥10 population

Statistical significance had to be reached in the first group (CPS ≥1) before formal testing could proceed to the next groups.

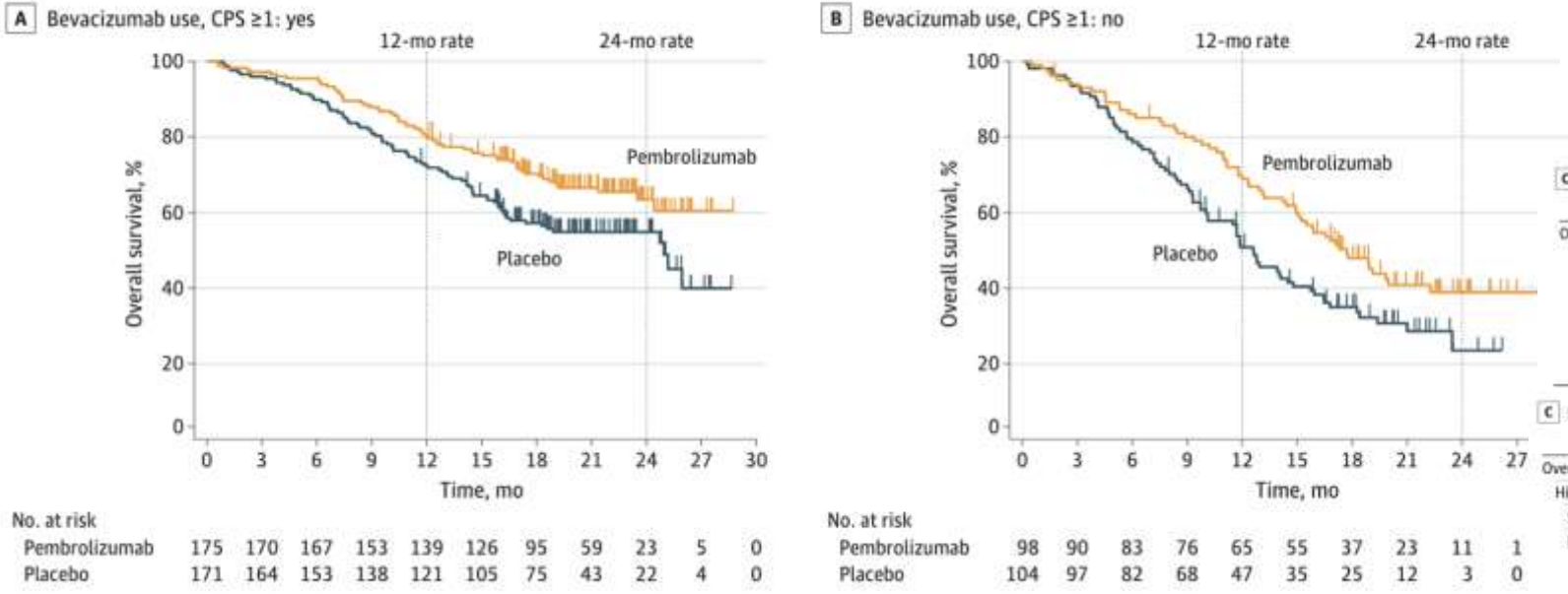
**Of note PDL1- population was 11% (69)!!!**

| Subgroup | Median PFS (mo) | HR for PFS (95% CI) | Median OS (mo) | HR for OS (95% CI) | p-value* |
|---|---|---|---|---|---|
| ITT (all comers) | 10.4 vs 8.2 | 0.61 (0.50–0.74) | 26.4 vs 16.8 | 0.63 (0.52–0.77) | < 0.0001 |
| CPS ≥ 1 | 10.5 vs 8.2 | 0.58 (0.47–0.71) | 28.6 vs 16.5 | 0.60 (0.49–0.74) | < 0.0001 |
| CPS ≥ 10 | 10.4 vs 8.1 | 0.52 (0.40-0.68) | 29.6 vs 17.4 | 0.58 (0.44–0.78) | < 0.0001 |
| CPS < 1 | NR | 0.95 (0.52–1.70) | No benefit | 0.87 (0.50–1.52) | NS |

# KEYNOTE-826 sub-group analysis

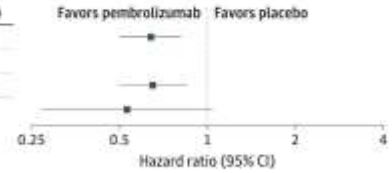
## 228 (37%) did not receive Bev

**Figure 2. Overall Survival by Bevacizumab Use**



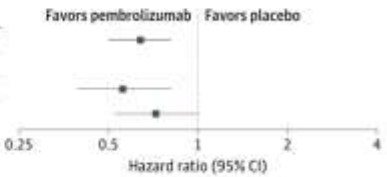

C Subgroup analysis of overall survival by choice of platinum, CPS ≥1

| | No. of events | No. of patients | HR for death (95% CI) |
|---|---|---|---|
| Overall | 272 | 548 | 0.64 (0.50-0.81) |
| Platinum use | | | |
| Carboplatin | 231 | 447 | 0.65 (0.50-0.85) |
| Cisplatin | 39 | 99 | 0.53 (0.27-1.04) |



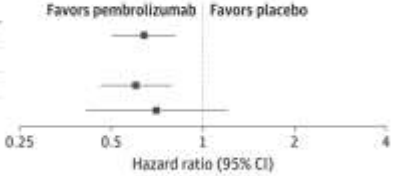

C Subgroup analysis of overall survival by prior CRT only, CPS ≥1

| | No. of events | No. of patients | HR for death (95% CI) |
|---|---|---|---|
| Overall | 272 | 548 | 0.64 (0.50-0.81) |
| Prior CRT only | | | |
| Yes | 118 | 215 | 0.56 (0.39-0.81) |
| No | 154 | 333 | 0.72 (0.52-1.00) |




C Subgroup analysis of overall survival by histology, CPS ≥1

| | No. of events | No. of patients | HR for death (95% CI) |
|---|---|---|---|
| Overall | 272 | 548 | 0.64 (0.50-0.81) |
| Histology | | | |
| Squamous | 213 | 409 | 0.60 (0.46-0.79) |
| Nonsquamous | 59 | 138 | 0.70 (0.41-1.20) |




*Tewari KS et al., JAMA 2024*

# Clinical impact

**CT backbone (Platinum + Taxane)**

GOG 204 established the standard: median OS 12.9 months

ORR 29%

**Adding Bevacizumab**

GOG 240 added Bev: median OS 17.5 months

ORR 48%

**Adding Pembrolizumab**

KEYNOTE-826 added Pembro: median OS 28.6 months (in CPS

ORR 69%

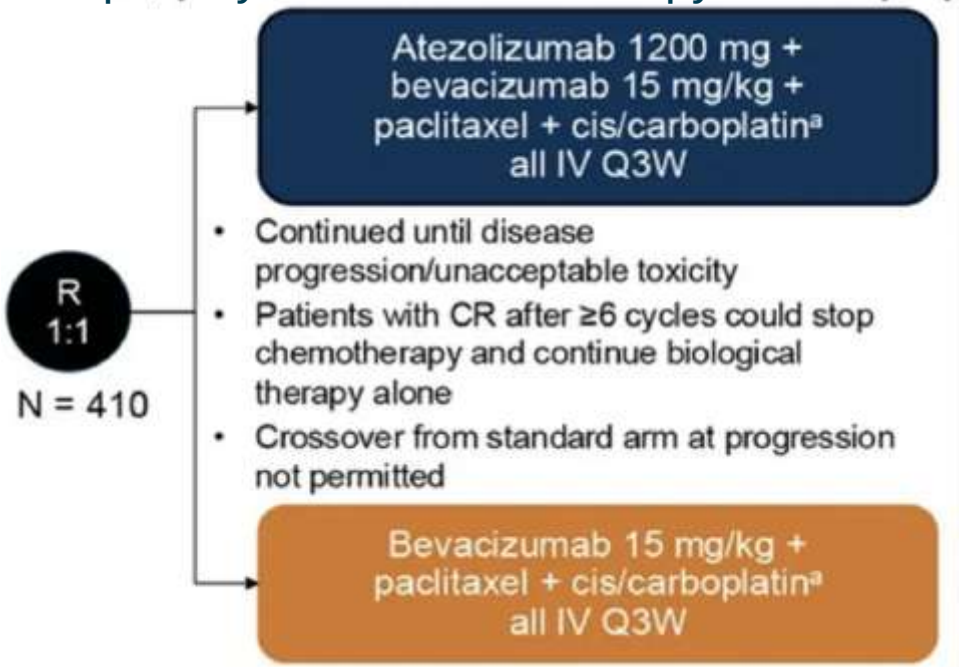
*Monk BJ et al., JCO 2009, Tewari KS et al., Lancet 2017, Monk BJ et al., JCO 2023*

# BEATcc (Updated Data from 2025 ESMO-gyn)

ESMO GYNAECOLOGICAL CANCERS
VIENNA AUSTRIA
19-21 JUNE 2025

Key Eligibility Criteria

- P/R or M CC not amenable to curative treatment
- No prior systemic chemotherapy for R/M CC




Stratification factors

- Prior concurent chemoradiation (yes vs no)
- Histology
- Chemotherapy backbone (cisplatin vs carboplatin)

- Efficacy of Atezo + Beva + CT was confirmed in CC regardless of PD-L1 CPS status
  **No PD-L1 selection needed**

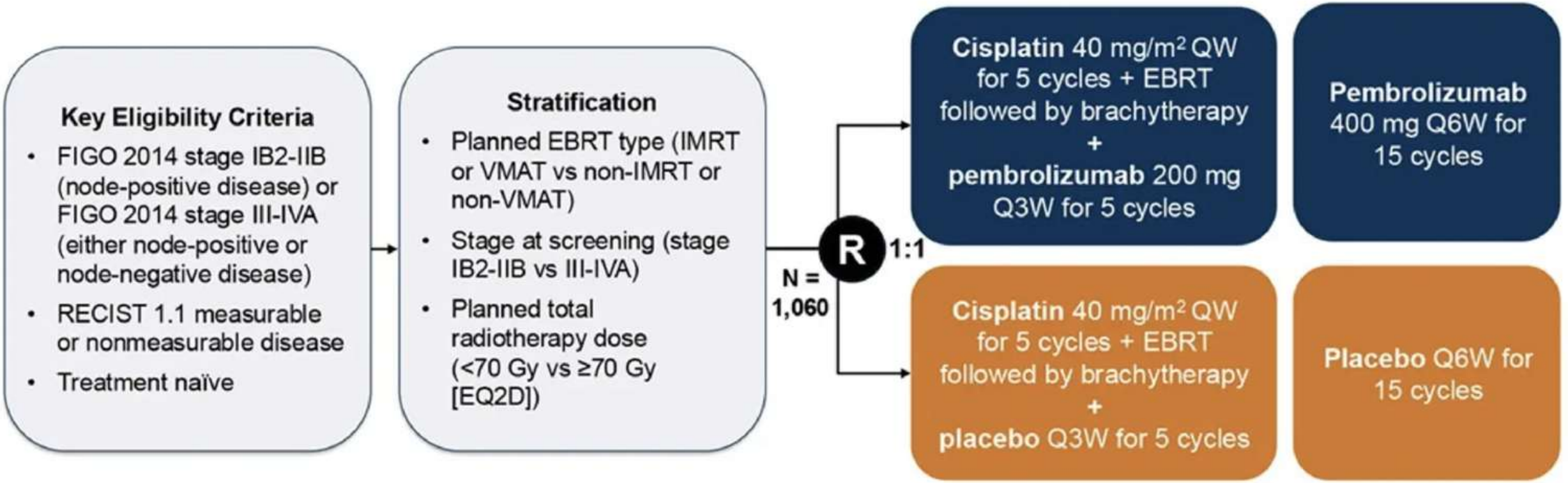
- **Progression-Free Survival (PFS):**
  CPS ≥1: 16.6 vs 10.5 months (HR 0.54)
  CPS <1: 13.6 vs 10.2 months (HR 0.48)

- **Overall Survival (OS)**
  Interim analysis: 33.2 vs 37.3 months

- **Definitive OS results expected in 2026**

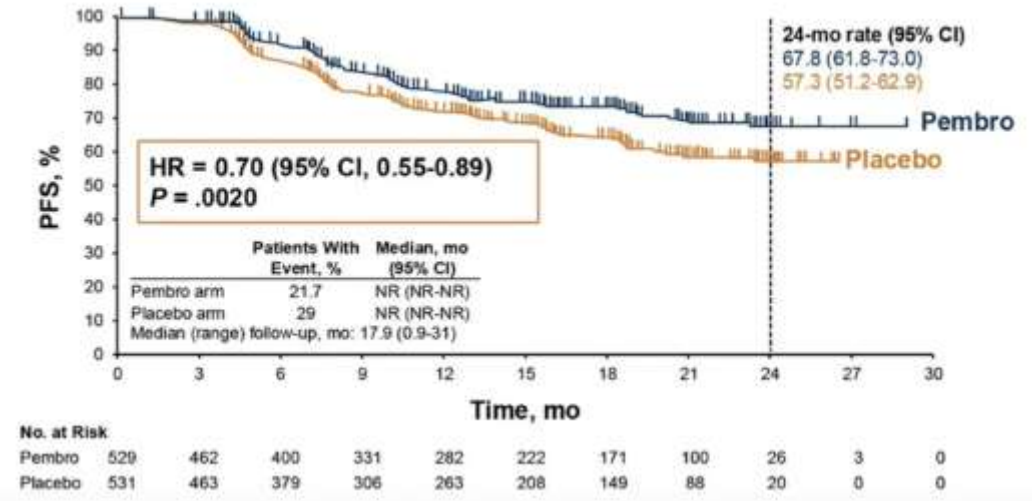
*Giorgi U et al., ESMO Gyn 2025*

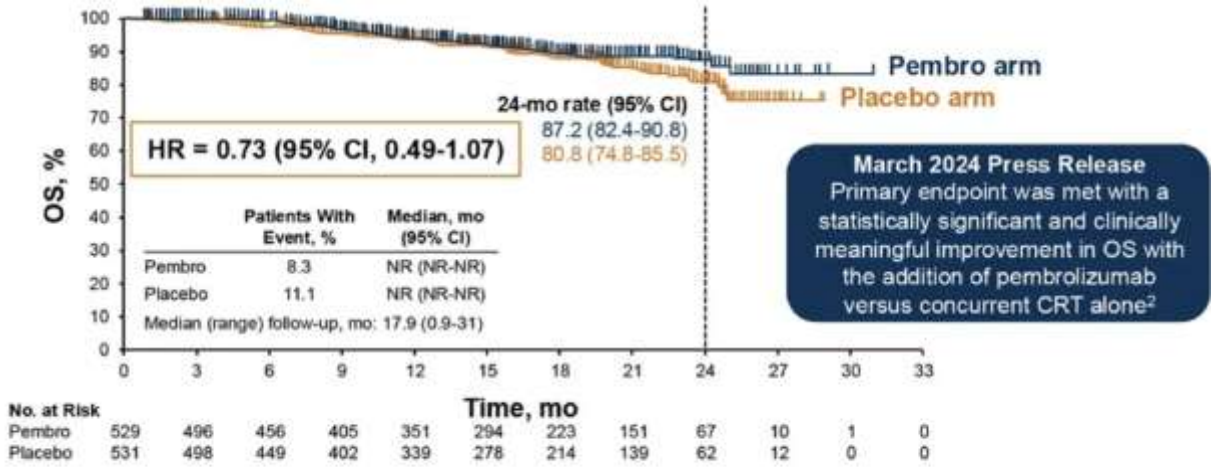
# KEYNOTE-A18




- **Primary endpoints:** PFS (per RECIST v1.1) by investigator or histopathologic confirmation and OS
- **Secondary endpoints:** 24-mo PFS, ORR, patient-reported outcomes, and safety

# KEYNOTE-A18



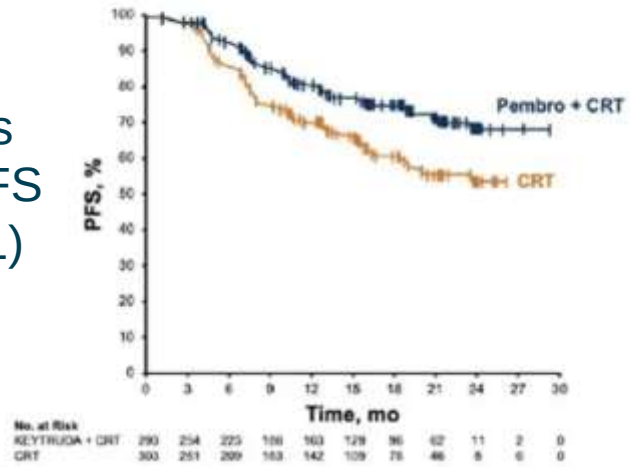




**March 2024 Press Release**
Primary endpoint was met with a statistically significant and clinically meaningful improvement in OS with the addition of pembrolizumab versus concurrent CRT alone[2]

## III-IVA CC pts

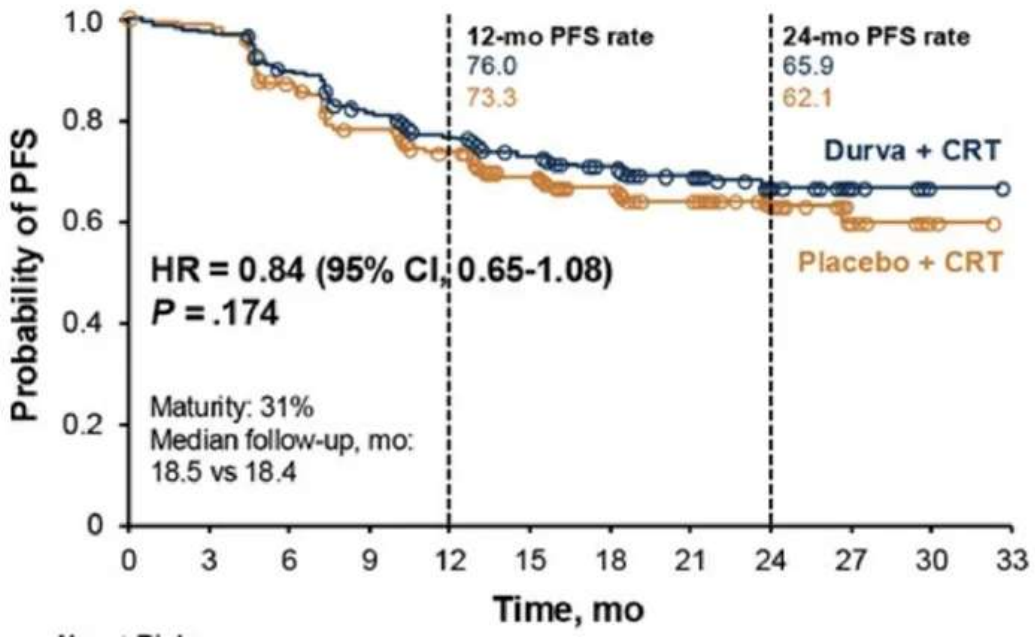
In an exploratory analysis for the 462 pts with FIGO Stage IB2-IIB disease, the PFS HR estimate was 0.91 (95%CI, 063-1.31)

**Kaplan-Meier Curve for PFS in KEYNOTE-A18 (Patients With FIGO 2014 Stage III-IVA Cervical Cancer)**

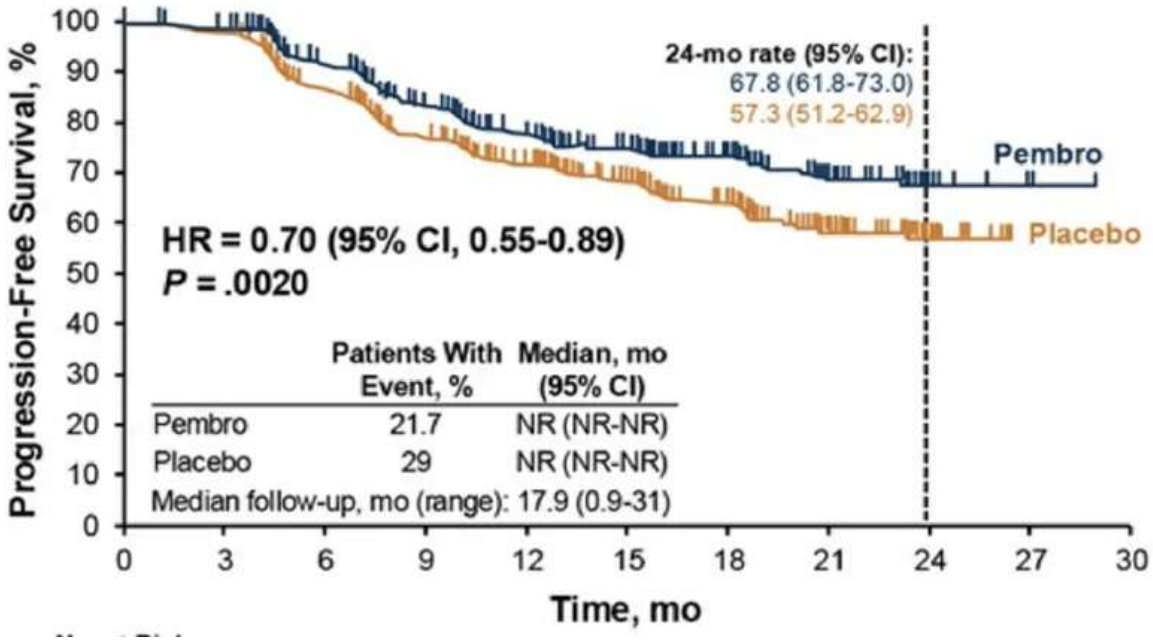



| | Pembrolizumab 200 mg Q3W and 400 mg Q6W + CRT (n = 293) | Placebo + CRT (n = 303) |
|---|---|---|
| **PFS by investigator** | | |
| Patients with event, n (%) | 61 (21) | 94 (31) |
| Median, mo (95% CI) | NR (NR-NR) | NR (18.8-NR) |
| 12-mo PFS rate (95% CI) | 81 (75-85) | 70 (64-76) |
| HR (95% CI) | 0.59 (0.43-0.82) | |

## Durvalumab in CALLA[1]




## Pembrolizumab in KEYNOTE-A18[2]




CALLA enrolled a lower-risk population: Positive para-aortic lymph nodes: ~10% in CALLA vs ~22% in KEYNOTE-A18
Number of progression or death events at primary analysis: comparable ~227 events in CALLA vs ~237 events in KEYNOTE-A18

Data maturity: similar

Median follow-up: 18.5 months (CALLA) vs 17.9 months (KEYNOTE-A18)

**CALLA studied an anti–PD-L1 Ab (durvalumab) and KEYNOTE-A18 an anti–PD-1 Ab (pembrolizumab)**

# Other settings??? -NACT-

| Agent(s) | Phase & Status | Regimen | ORR (Objective RR) | Key Notes |
|---|---|---|---|---|
| Camrelizumab + chemotherapy | Phase II (NACI) – completed | 1 priming chemo → 2 chemo + camrelizumab in LACC | 98% (95% CI 95.4–100%)19% pCR | Includes high ORR 98%; CR 19% |
| Tislelizumab + chemotherapy | Phase II – completed/ongoing | 3 cycles PD-1 inhibitor + chemotherapy followed by surgery | 87.0% (56.5% CR + 30.5% PR) 60.9% pCR | 60.9% pCR in surgical specimens; safe & manageable toxicity |
| Pembrolizumab (MITO CERV-3) | Phase II | 3 cycles chemo + Pembro, if response→surgery | N/A (pilot phase) | PFS |
| Cadonilimab | Phase II | 3 cycles + Cadonilimab, if response→surgery | NA | ORR and pCR |

# Immunotherapy in CC: ongoing trials

| Trial | Agent | Setting | Phase | Primary endpoint | Patients |
|---|---|---|---|---|---|
| ENGOT-cx13 / NCT03912415 | BCD-100 Anti-PD-1 ± chemo ± Beva | Recurrent/metastatic | III | OS | 316 |
| ATEZOLACC / NCT03612791 | Atezolizumab + CCRT | LACC | II | PFS | 189 |
| NCT05492123 | Nivolumab + Ipilimumab + CCRT | LACC high-risk | II | 3-yr PFS | 112 |
| NCT04865887 | Pembrolizumab + Lenvatinib | Recurrent/metastatic | II | ORR | 35 |
| NCT06099418 | Vaccine (VB10.16) + Atezolizumab/placebo | Refractory to Pembro + chemo | II | ORR | 130 |
| NCT03444376 | Vaccine (GX-188°) + Pembrolizumab/placebo | Refractory to Pembro + chemo +/- Beva | I/II | ORR | 60 |
| NCT04380805 | Cadonilimab Anti-PD-1 | Recurrent/metastatic after chemo | II | ORR | 30 |
| NCT04483544 | Pembro + Olaparib | Recurrent/metastatic on chemo | II | ORR | 48 |
| GOTIC-025/ NCT04641728 | Pembro + Olaparib | Recurrent/metastatic after chemo | II | ORR | 28 |
| NCT04652076 | NP137 (anti-Netrin-1)+ Pembro + TC | Recurrent/metastatic after chemo | I/II | ORR | 240 |
| NCT03972722 | Zimberelimab + CCRT ± chemo | Neoadjuvant zimberelimab with radiation ± chemotherapy | I/II | ORR | 19 |

# Immunotherapy Rechallenge with Cadonilimab in Patients with Recurrent or Metastatic Cervical Cancer : A Retrospective Study

SGO
ANNUAL MEETING
ON WOMEN'S CANCER
SEATTLE, WA • 2025

**Objective**

- To investigate the efficacy and safety of cadonilimab in R/M CC with disease progression after monoclonal antibody failure

**Design**

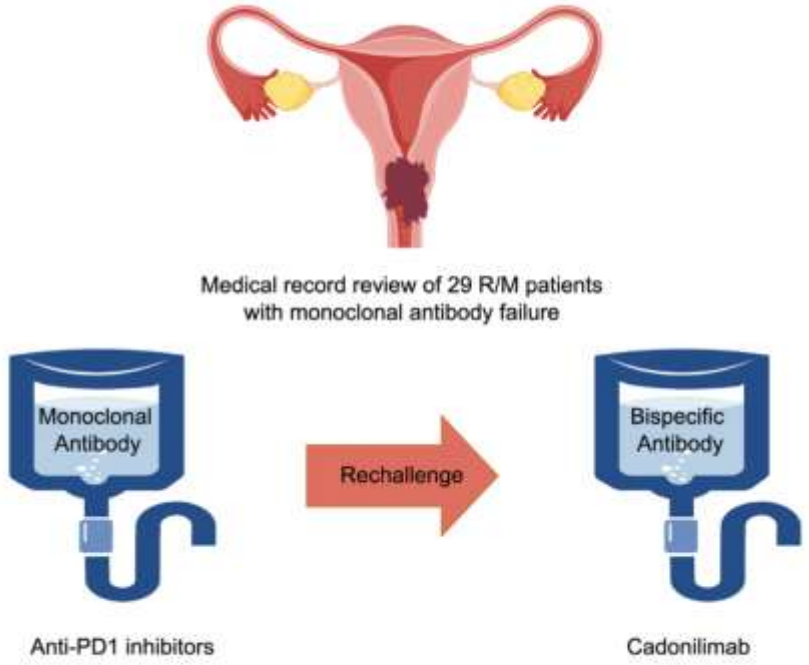
- A retrospectively observation study

**Participants**

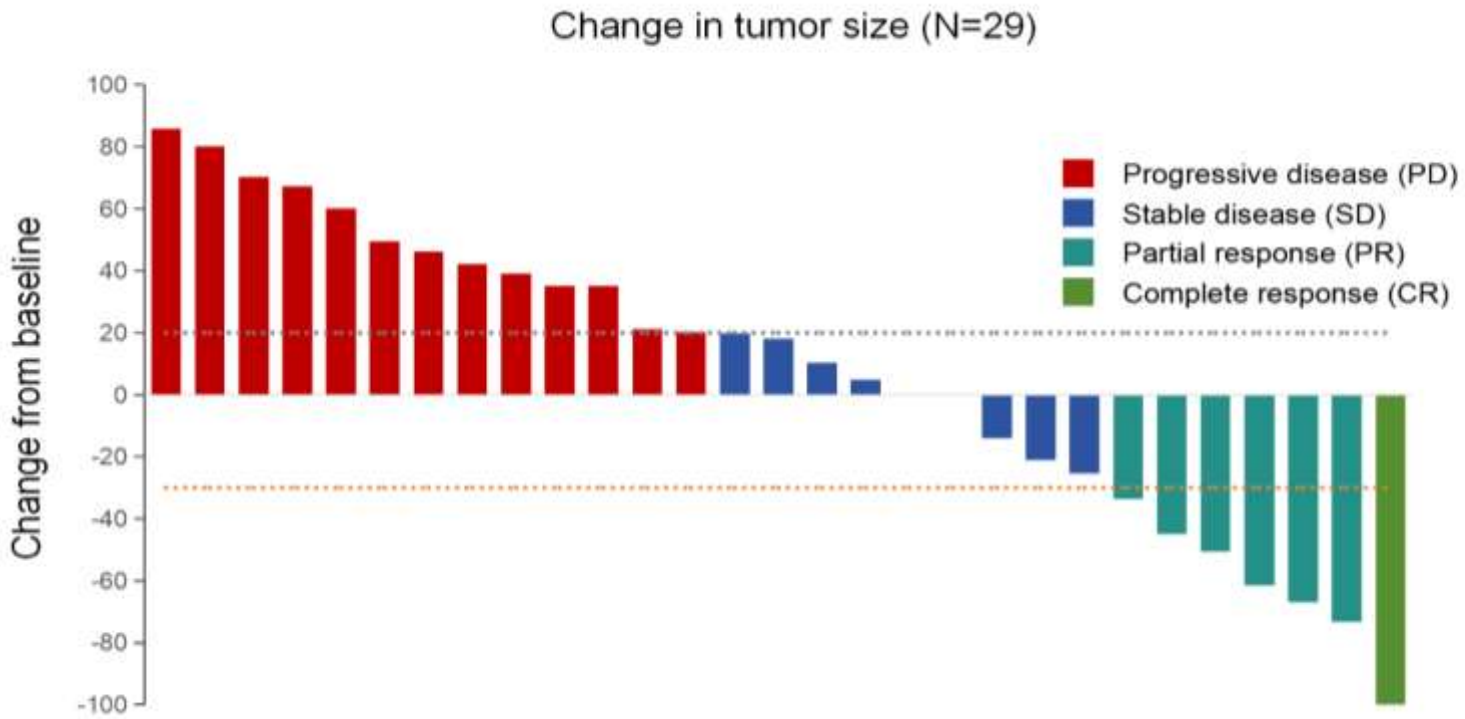
- 29 R/M CC patients

**Assessment**

- ORR、DCR、OS、PFS、Safety



# Immunotherapy Rechallenge with Cadonilimab in Patients with Recurrent or Metastatic Cervical Cancer : A Retrospective Study




| Response | Patients (%) | | |
|---|---|---|---|
| | All (n=29) | CPS ⩾1% (n=9) | CPS < 1% (n=4) |
| CR | 1(3.4) | 1(11.1) | 0(0) |
| PR | 6(20.7) | 3(33.3) | 1(25.0) |
| SD | 9(31.0) | 2(22.2) | 2(50.0) |
| PD | 13(44.8) | 3(33.3) | 1(25.0) |
| ORR | 7(24.1) | 4(44.4) | 1(25.0) |
| DCR | 16(55.2) | 6(66.7) | 3(75.0) |

# Zimberelimab Combo Elicits Activity in Previously Treated Cervical Cancer

March 15, 2025
By Russ Conroy
Fact checked by Tim Cortese

Conference | Society of Gynecologic Oncology Annual Meeting on Women's Cancer (SGO)

SGO ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025

*News* *Article*

*Combining zimberelimab with lenvatinib produced a manageable safety profile among patients with advanced cervical cancer in a phase 2 trial.*

Treatment with zimberelimab plus lenvatinib (Lenvima) demonstrated promising clinical activity in a small cohort of patients with advanced cervical cancer who experienced disease progression on prior treatment with immune checkpoint inhibitor (ICI) therapy, according to findings from a phase 2 trial (NCT05824468) presented at the **2025 Society of Gynecologic Oncology Annual Meeting on Women's Cancer (SGO).**[1]

*"Zimberelimab plus lenvatinib showed promising antitumor activity in patients with advanced cervical cancer who have experienced disease progression after prior ICI therapy," according to study author Chunyan Lan, MD, PhD.*

Among 30 evaluable patients, study treatment yielded an objective response rate (ORR) of 33.3% (95% CI, 17.3%-52.8%), which consisted entirely of partial responses (PRs). Data also showed a disease control rate (DCR) of 96.7% (95% CI, 82.8%-99.9%)

# Take home messages and open questions

☑ Take-Home Messages:

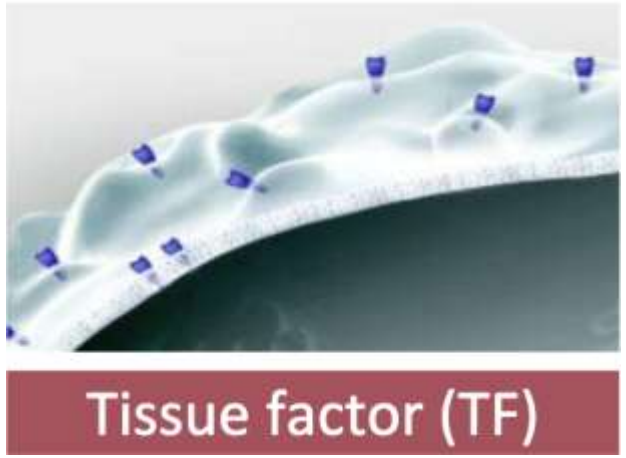
- Immunotherapy is now a standard in recurrent/metastatic and locally advanced disease.
- Checkpoint inhibitors improve OS, especially in PD-L1 positive tumors.
- Benefit observed across histologies and PD-L1 status.
- Long-term data confirm sustained survival and manageable safety.
- Investigational combinations include ADCs and earlier lines of therapy.

? Open Questions:

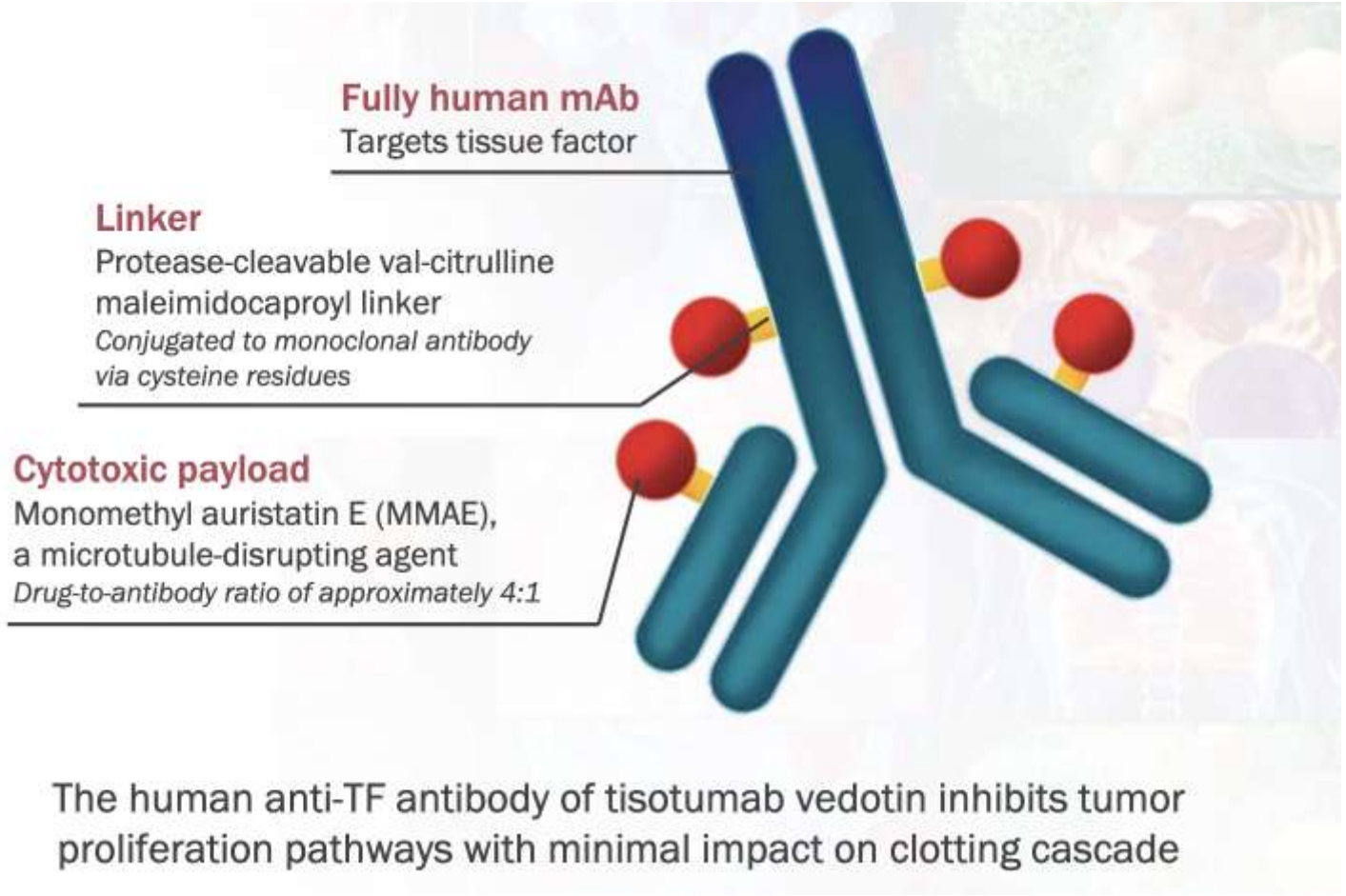
- What is the optimal duration of immunotherapy?
- Can we better select patients beyond PD-L1?
- Is there a role in PD-L1 negative or early-stage disease?
- How to ensure access in low-resource settings, where disease burden is highest?
- Can vaccines, TILs, or bispecifics further improve outcomes?


with **NEW DRUGS**

# TISOTUMAB VEDOTIN

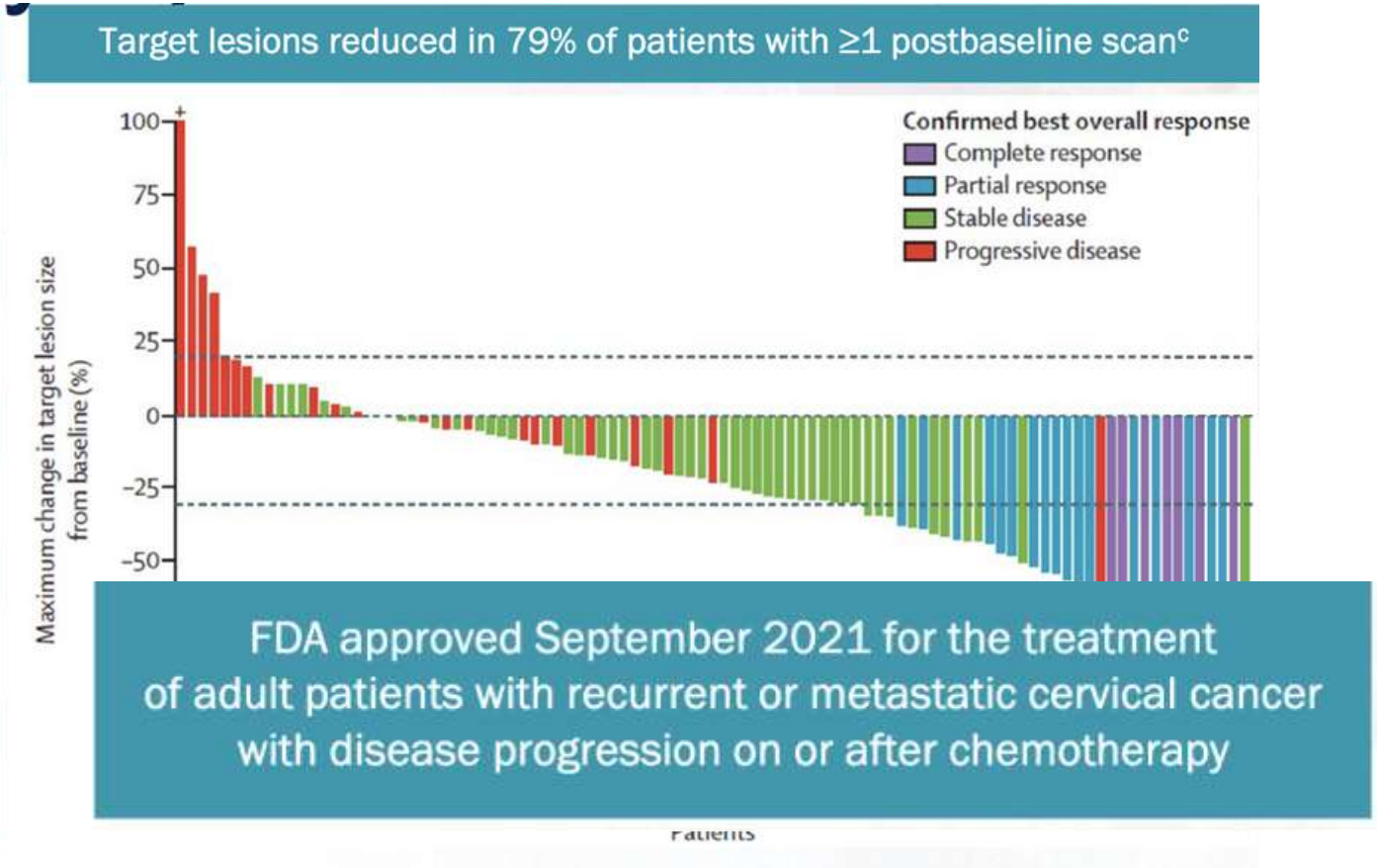



- Transmembrane protein: main physiological initiator of coagulation1
- Role in oncogenesis includes angiogenesis, cell adhesion, motility, and cell survival 2
- Highly expressed in many solid tumors including cervical, ovarian, pancreatic, SCCHN, NSCLC, and others3-7
- Expression associated with poor clinical outcomes, tumor initiation, progression, angiogenesis, and metastasis2



# InnovaTV 204/GOG-3023/ENGOT-cx6: Phase 2 Global Trial of Tisotumab Vedotin

| Response rates by IRC assessment | (N=101) |
|---|---|
| ORR[a] (95% CI), % | 24 (16-33) |
| CR, no. (%) | 7 (7) |
| PR, no. (%) | 17 (17) |
| SD, no. (%) | 49 (49) |
| PD, no. (%) | 24 (24) |
| Not evaluable, no. (%) | 4 (4) |
| Disease control rate[b] (95% CI), % | 72 (63-81) |
| Median DOR (95% CI), mo | 8.3 (4.2-NR) |
| Median time to response (IQR), mo | 1.4 (1.3-1.5) |
| Median PFS (95% CI), mo | 4.2 (3.0-4.4) |

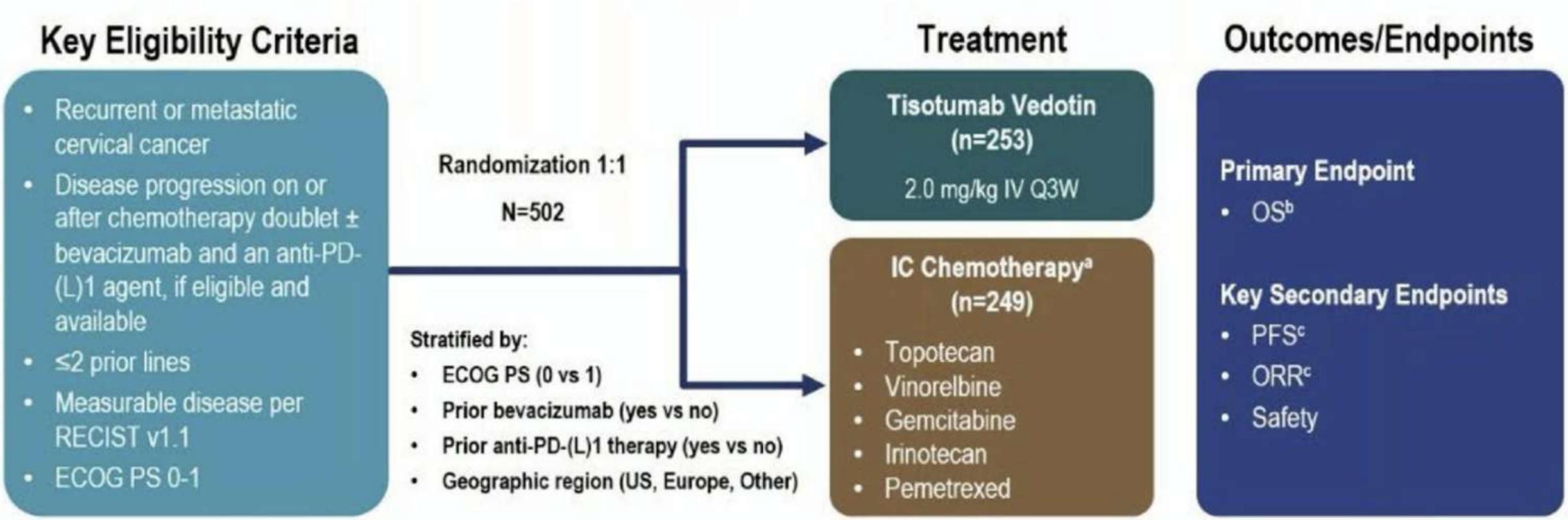



Median follow-up: 10.0 months.

a Based on the Clopper-Pearson method. b Disease control rate is the proportion of patients with a confirmed CR, PR, or SD. c Percent changes greater than 100% were truncated at 100% (indicated by the + symbol).

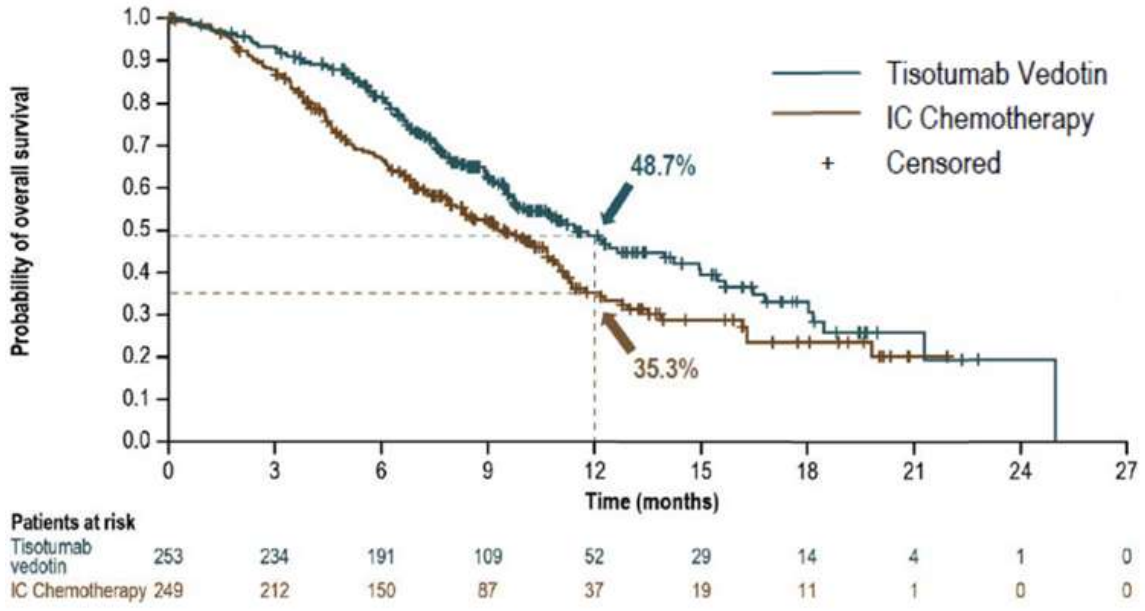
*Coleman R et al., Lancet Oncol 2021*

# InnovaTV 301 a randomized, open label phase III trial

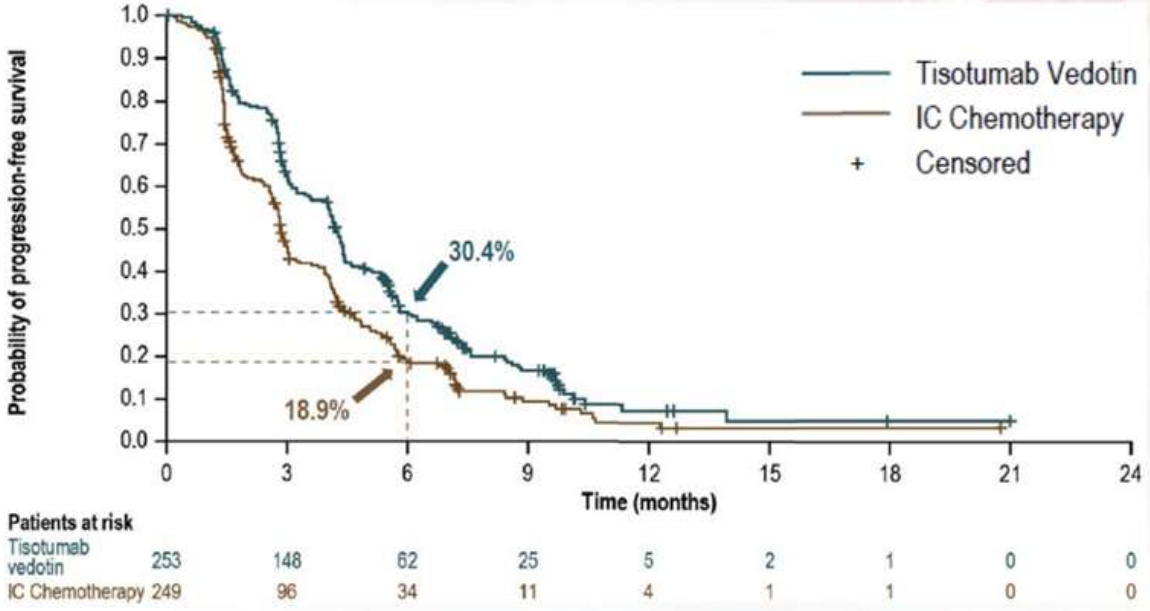


# InnovaTV 301 a randomized, open label phase III trial

| | Events/ Total | mOS (95% CI) | HR (95% CI) | Stratified log-rank P value[a] |
|---|---|---|---|---|
| TV | 123/253 | **11.5** (9.8-14.9) | **0.70** (0.54-0.89) | 0.0038 |
| Chemo | 140/249 | **9.5** (7.9-10.7) | | |



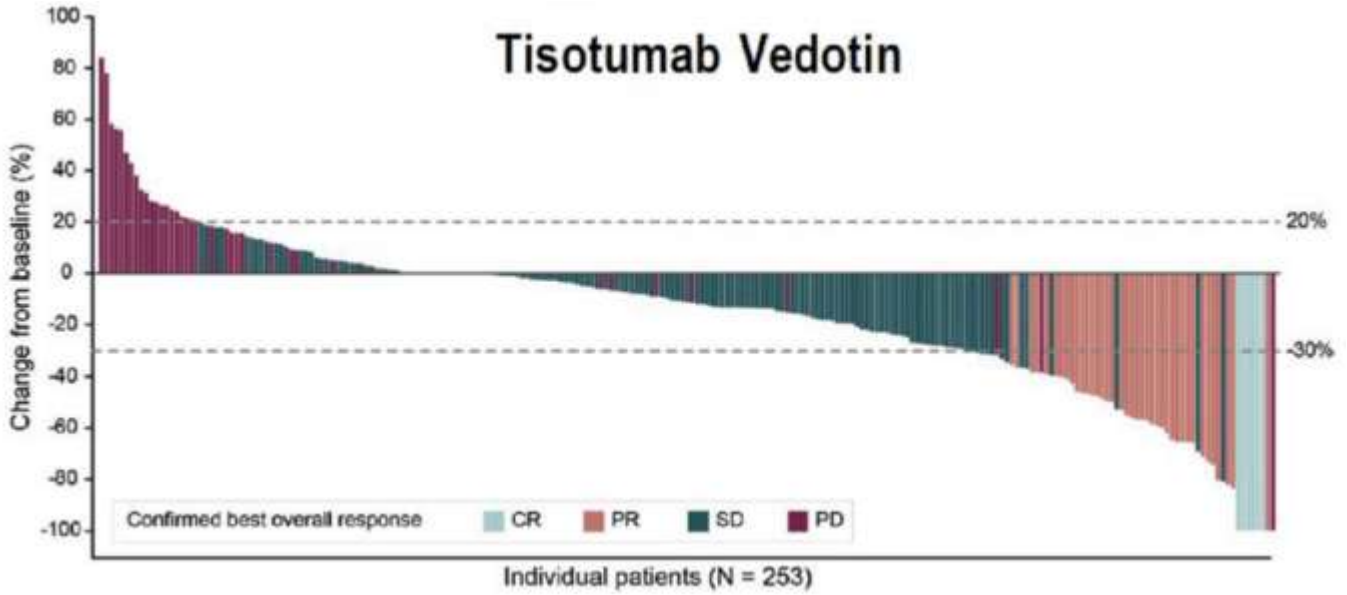

| | Events/ Total | mPFS (95% CI) | HR (95% CI) | Stratified log-rank P value[b] |
|---|---|---|---|---|
| TV | 198/253 | **4.2** (4.0-4.4) | **0.67** (0.54-0.82) | <0.0001 |
| Chemo | 194/249 | **2.9** (2.6-3.1) | | |




*Vergote I, et al. ESMO 2023*

# InnovaTV 301 a randomized, open label phase III trial

| | TV (N=253) | Chemo (N=249) |
|---|---|---|
| ORR, % (95% CI) | **17.8** (13.3-23.1) | **5.2** (2.8-8.8) |
| Odds ratio (95% CI) | 4.0 (2.1-7.6) | |
| *P* value | <0.0001 | |




Press release

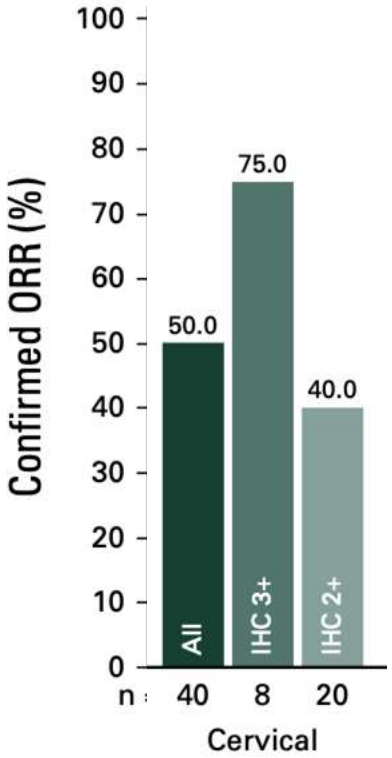
| Population | Median OS (months) | HR (vs chemo) | P value |
|---|---|---|---|
| Global (innovaTV-301) | 11.5 (95% CI 9.8–14.9)<br>vs<br>9.5 (95% CI 7.9–10.7) | 0.70 (95% CI 0.54–0.89) | 0.0038 |
| China Subgroup | NR<br>vs<br>10.7 (95% CI 6-NR) | 0.55 (95% CI 0.27–1.15) | Not Reported |

*Vergote I, et al. ESMO 2023*

Original Reports | Gynecologic Cancer

Check for updates

# Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial




- HER2-positive cervical cancer patients in DESTINY-PanTumor02 achieved:

- 50% Objective Response Rate (ORR) overall, rising to 75% in those with IHC 3+ HER2 expression
- Median PFS not reached in IHC 3+; 4.8 mo in IHC 2+ group
- Median OS of 21.1 mo (95% CI: 15.3–29.6) in IHC 3+ patients

| Study | Agent | Population | ORR | Median PFS | Median OS |
|---|---|---|---|---|---|
| DESTINY-PanTumor02 | Trastuzumab deruxtecan | HER2+ cervix (IHC 3+) | 50% (up to 75% in IHC 3+) | NR (IHC 3+); 4.8 mo (IHC 2+) | 21.1 mo (IHC 3+; 95% CI: 15.3–29.6) |
| DESTINY-PanTumor02 | Trastuzumab deruxtecan | HER2+ cervix (IHC 2+) | n/a | 4.8 mo | — |

*Bernstam FM et al., JCO 2024*

# Sacituzumab Govitecan

**18**

**Sacituzumab govitecan for Chinese patients with recurrent/ metastatic cervical cancer: Interim analysis of the phase II basket study EVER-132-003**

Jusheng An[a], Guiling Li[b], Yunyan Zhang[c], Weimin Kong[d], Mei Feng[e], Cong Xu[f], Jusheng An[g], Long Ma[h], Simonetta Mocci[h], Lin Shen[i]. *[a]National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; [b]Union Hospital Affiliated to Tongji Medical College of Huanzhong University, Wuhan, China; [c]Harbin Medical University Cancer Hospital, Harbin, China; [d]Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China; [e]Fujian Cancer Hospital, Fuzhou, China; [f]Gilead Sciences Inc., Shanghai, China; [g]Gilead Sciences Inc., Beijing, China; [h]Gilead Sciences Inc., Foster City, CA, United States; [i]Peking University Cancer Hospital and Institute, Beijing, China*

**Conclusions**

This analysis in a small population demonstrates the promising efficacy and manageable safety of sacituzumab govitecan in Chinese patients with recurrent/metastatic cervical cancer with limited treatment options.

**Efficacy endpoints**

| | N=18 |
|---|---|
| ORR, n (%; 95% CI) | 9 (50; 26-74) |
| DCR, n (%; 95% CI) | 17 (94; 73-100) |
| DoR, months, median (95% CI) | 9.2 (2.9-not estimable) |
| PFS, months, median (95% CI) | 8.1 (4.1-10.6) |

*Jusheng An et al., Gynecol Oncol 2024*

# Ongoing trials with ADCs

| Trial / NCT | ADC Agent | Target | Setting | Phase | Primary Endpoint | Enrollment |
|---|---|---|---|---|---|---|
| ENGOT-cx8/GOG-3024/innovaTV 205/NCT03786081 | Tisotumab Vedotin + Pembrolizumab/ Bevacizumab/ Platinum | Tissue Factor | Recurrent/ Metastatic | I/II | ORR | 214 |
| innovaTV 301/ NCT04697628 | Tisotumab Vedotin | Tissue Factor | 2L/3L Recurrent/ Metastatic | III | OS | 502 |
| NCT05838521 | Sacituzumab Govitecan | Trop-2 | Recurrent/ Persistent | II | ORR | ~20 |
| NCT04482309 | Trastuzumab Deruxtecan | HER2 | HER2+ solid tumors | II | Safety/ORR | ~468 |
| NCT04965519 | Disitamab Vedotin | HER2 | HER2+ cervical cancer | I/II | ORR | ~120 |

# Ongoing trials with ADCs

| Patient population | Part 1: Dose escalation | Part 2: Dose expansion | Objectives |
|---|---|---|---|
| Recurrent or metastatic cervical cancer (N=~220) | 2L+ Arm A: TV (ED) q3w + bevacizumab (ED)<br>2L+ Arm B: TV (ED) q3w + pembrolizumab (FD)<br>2L+ Arm C: TV (ED) q3w + carboplatin (FD) | 1L Arm D: TV 2 mg/kg q3w + carboplatin<br>1L Arm E: TV 2 mg/kg q3w + pembrolizumab<br>2L/3L Arm F: TV 2 mg/kg q3w + pembrolizumab<br>2L/3L Arm G: TV 2 mg/kg days 1, 8, and 15 of a 28-day cycle<br>1L Arm H: TV 2 mg/kg q3w + pembrolizumab + carboplatin ± bevacizumab | Primary objectives<br>▪ Part 1: Safety and tolerability (DLTs, MTD, RP2D)<br>▪ Part 2: Antitumor activity (ORR by RECIST v1.1) |

ED=escalating dose; FD=fixed dose.

**Key eligibility criteria**

- Recurrent or metastatic cervical cancer
- Progressed on or after SOC therapy (arms A, B, and C only)
- No prior systemic therapy (arms D, E, and H only)
- Progressed on or after 1-2 prior systemic therapies (arms F and G only)
- ECOG PS 0-1

# Take home messages and open questions

☑ Take-home messages:

- Emerging treatments such as ADCs represent a promising strategy in P/R CC
- TV has shown activity in pre-treated populations with manageable toxicity.
- Combination strategies (e.g., ADCs + ICI or chemo) may improve efficacy.
- Target expression (e.g., tissue factor) is key for patient selection.
- ADCs may offer chemotherapy-free regimens and improved QoL.

? Open questions:

- What is the optimal sequencing of ADCs in the treatment pathway?
- How can we refine biomarkers to identify best responders?
- Will combination strategies lead to synergy or more toxicity?
- How can resistance to ADCs be overcome?
- How feasible is ADC use in LMICs, given cost and access issues?

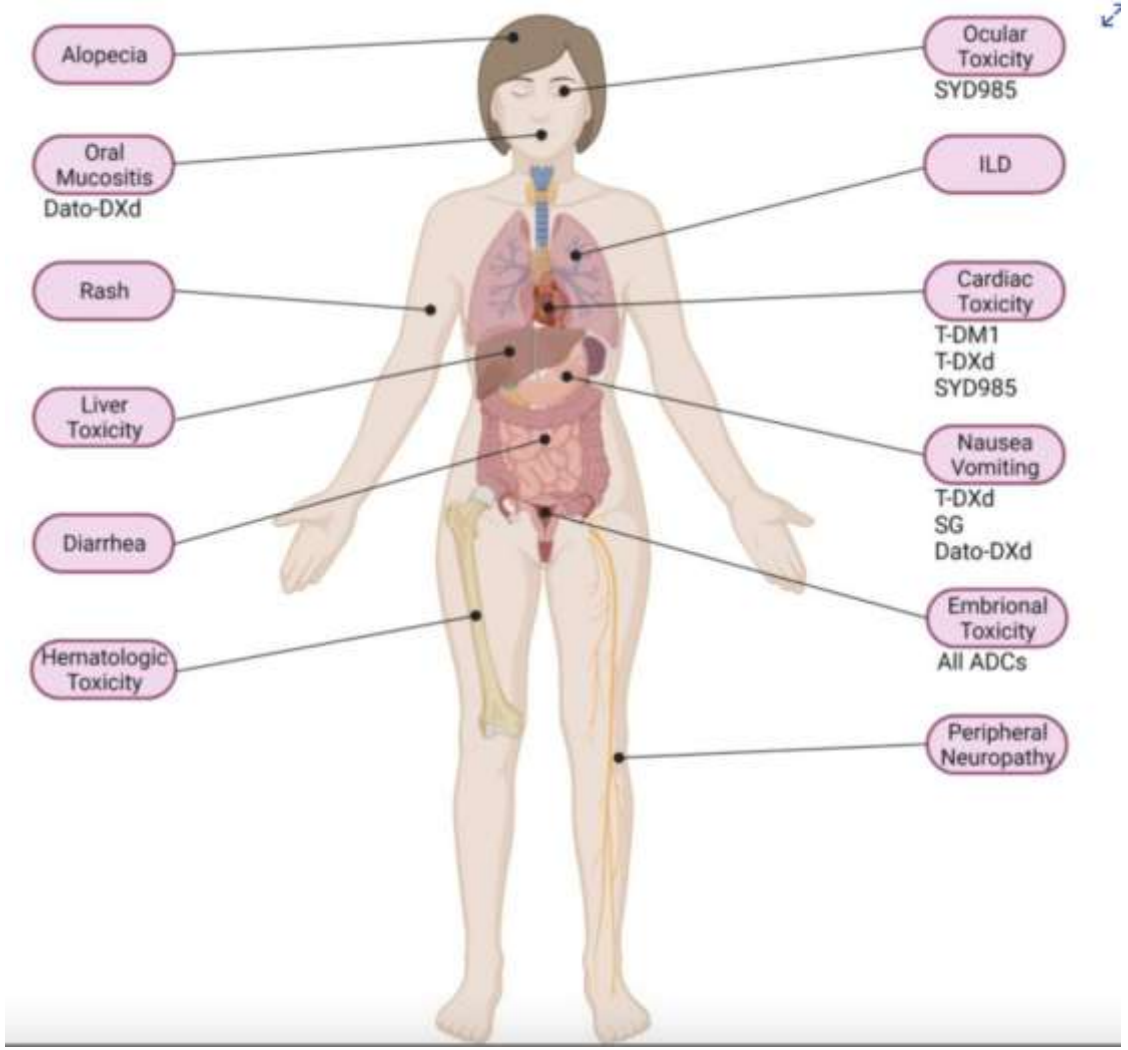
# Adverse events

**Table 2** Adverse events of advanced and recurrent cervical cancer patients

| Adverse events | Platinum and paclitaxel ($n=36$) | | | ICI plus platinum and paclitaxel ($n=33$) | | | *P* value* |
|---|---|---|---|---|---|---|---|
| | Total | Grade 1–2 | Grade 3–4 | Total | Grade 1–2 | Grade 3–4 | |
| Anemia, n (%) | 13 (36.1) | 11 (30.6) | 2 (5.5) | 14 (42.4) | 12 (36.3) | 2 (6.1) | 0.591 |
| Leukopenia, n (%) | 9 (25.0) | 9 (25.0) | 0 (0.0) | 11 (33.3) | 10 (30.3) | 1 (3.0) | 0.446 |
| Fatigue, n (%) | 10 (27.8) | 9 (25.0) | 1 (2.8) | 10 (30.3) | 10 (30.3) | 0 (0.0) | 0.817 |
| Nausea and vomiting, n (%) | 9 (25.0) | 8 (22.2) | 1 (2.8) | 10 (30.3) | 9 (27.3) | 1 (3.0) | 0.622 |
| Diarrhea, n (%) | 8 (22.2) | 8 (22.2) | 0 (0.0) | 9 (27.3) | 9 (27.3) | 0 (0.0) | 0.627 |
| Anorexia, n (%) | 6 (16.7) | 6 (16.7) | 0 (0.0) | 8 (24.2) | 8 (24.2) | 0 (0.0) | 0.434 |
| Neutropenia, n (%) | 7 (19.4) | 6 (16.7) | 1 (2.7) | 7 (21.2) | 6 (18.2) | 1 (3.0) | 0.855 |
| Peripheral neuropathy, n (%) | 4 (11.1) | 3 (8.3) | 1 (2.8) | 7 (21.2) | 5 (15.2) | 2 (6.0) | 0.252 |
| Constipation, n (%) | 10 (27.8) | 10 (27.8) | 0 (0.0) | 6 (18.2) | 6 (18.2) | 0 (0.0) | 0.345 |
| Pruritus, n (%) | 8 (22.2) | 8 (22.2) | 0 (0.0) | 6 (18.2) | 6 (18.2) | 0 (0.0) | 0.677 |
| Hypertension, n (%) | 7 (19.4) | 7 (19.4) | 0 (0.0) | 6 (18.2) | 5 (15.2) | 1 (3.0) | 0.893 |
| Thrombocytopenia, n (%) | 6 (16.7) | 6 (16.7) | 0 (0.0) | 4 (12.1) | 4 (12.1) | 0 (0.0) | 0.737 |
| Urinary tract infection, n (%) | 5 (13.9) | 5 (13.9) | 0 (0.0) | 4 (12.1) | 4 (12.1) | 0 (0.0) | 1.000 |
| Arthralgia, n (%) | 4 (11.1) | 4 (11.1) | 0 (0.0) | 3 (9.1) | 3 (9.1) | 0 (0.0) | 1.000 |
| Hypothyroidism, n (%) | 2 (5.6) | 2 (5.6) | 0 (0.0) | 3 (9.1) | 3 (9.1) | 0 (0.0) | 0.665 |

ICI, immune checkpoint inhibitor

*,Comparison of the occurrence of adverse events between advanced and recurrent cervical cancer patients with different treatments




**LET's know them!!!!**

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**Violante Di Donato**
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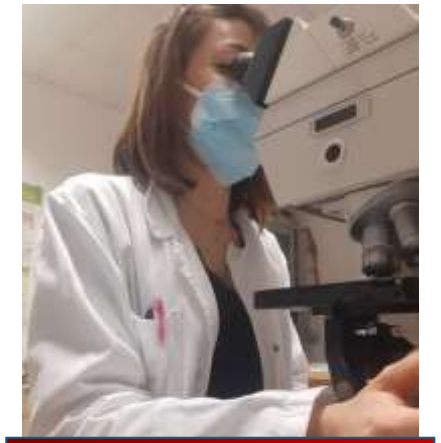

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