



ASGO Webinar #62

Asian Society of Gynecologic Oncology

Review course 2025: first session of the Year

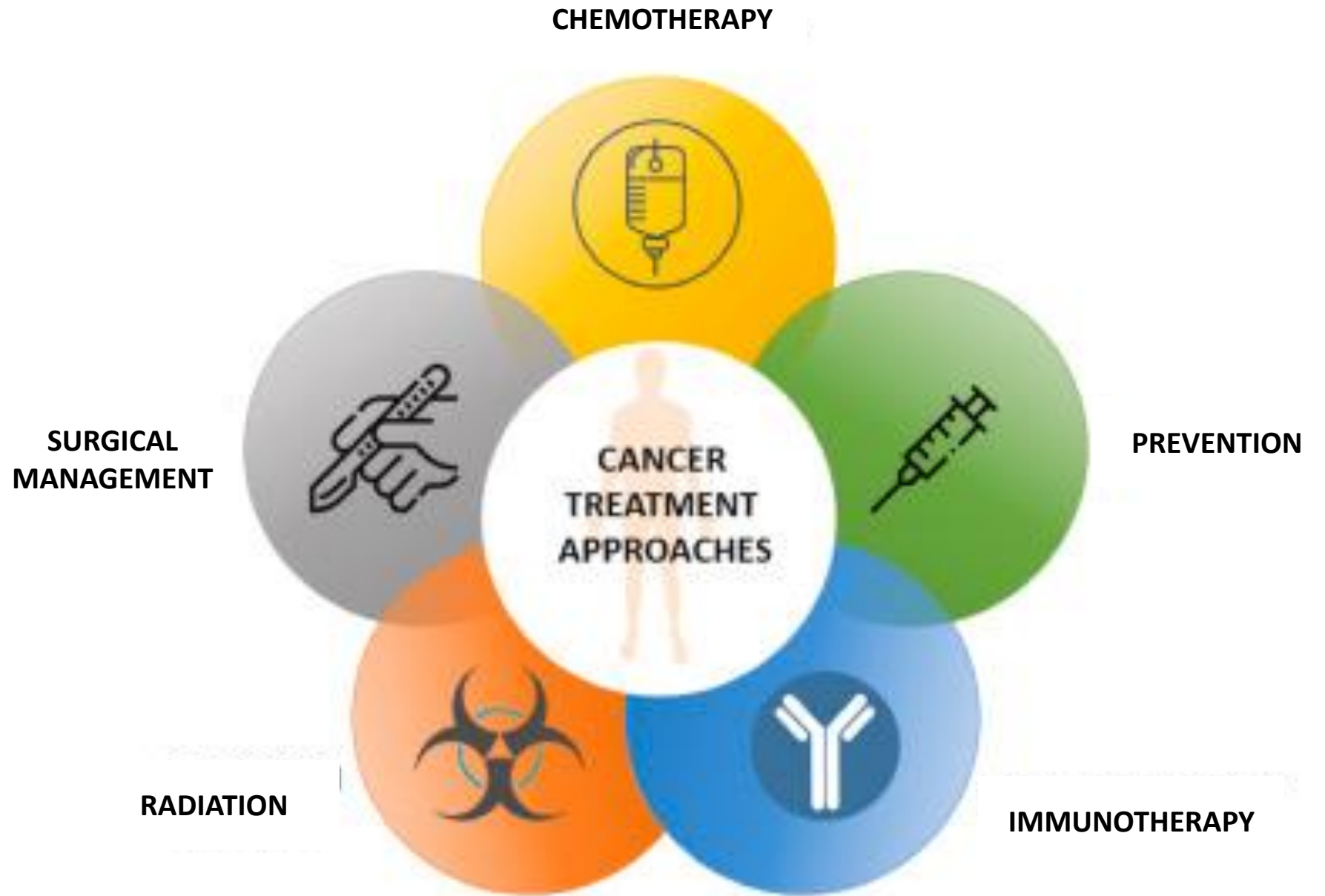
Cervical Cancer

24 July 2025

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India

Cervical Cancer



From **de-escalation in early-stage surgery to escalation of systemic therapy in LACC**, recent trials mark a paradigm shift—**tailoring treatment intensity** to tumor biology and patient risk

Prevention

OPEN

J Lower Gent Tract Dis April 2025

Updated Review for Guidelines for Cervical Cancer Screening in Immunosuppressed Women Without HIV Infection

Anna-Barbara Moscicki et al

Main Objective

- To evaluate new evidence about the risk of HPV infection, squamous intraepithelial lesions (SIL), and cervical cancer (CC) in non-HIV immunocompromised women, including those with:
 - Solid Organ Transplant (SOT)
 - End-Stage Renal Disease (ESRD)
 - Hematopoietic Stem Cell Transplant (HSCT)
 - Autoimmune Diseases (SLE, RA, IBD, MS)
 - Users of Disease-Modifying Therapies (DMTs) or Monoclonal Antibodies (MABs)
- It also updates screening and vaccination recommendations based on risk stratification, treatment status, and immunogenicity of HPV vaccines

Key Updated Screening Recommendations

Groups Requiring Enhanced Screening:

- Even if not HIV-positive, these groups are at increased risk:
 - SOT: Higher rates of HPV, SIL, and CC
 - ESRD: Dialysis patients have increased CC incidence
 - HSCT: Increased HPV-related cancer risk, including in those with GVHD
 - SLE: High HPV prevalence and CC risk regardless of immunosuppressant use
 - RA, IBD, MS: If on immunosuppressants or DMT/MABs, apply enhanced screening
- ✓ Enhanced screening - cytology annually until 3 consecutive normal results, followed by testing every 3 years
 - Cotesting is preferred if over age 30

Shared Decision-Making Recommended For

- RA, IBD, MS not on immunosuppressants
- All patients on DMTs or MABs (due to conflicting/inconclusive data)

No Enhanced Screening Recommended (General Population Guidelines Apply):

- RA, IBD, and MS patients not on immunosuppressants, unless shared decision-making leads otherwise

HPV Vaccine Recommendations

- 3-dose series recommended for all immunocompromised populations
 - Start vaccination at age 9; routine catch-up until age 26.
 - Shared decision-making applies from ages 27–45 per ACIP guidelines.
 - Best if initiated before starting immunosuppressive therapy, DMT, or transplant
 - Re-vaccination post-HSCT is recommended due to potential loss of immune memory
-
- Lower seroconversion rates in SOT, HSCT, and some autoimmune groups (e.g., SLE)
 - Vaccine is safe, but immune response is attenuated by certain immunosuppressants
 - Timing of vaccine (before treatment vs. post-treatment) impacts effectiveness
 - Data on vaccine efficacy in preventing CIN or CC in immunocompromised patients is still lacking

Summary

- This updated review recommends expanded cervical cancer screening and vaccination protocols for non-HIV immunocompromised women, aligning many groups with the HIV-based CDC guidelines due to equivalent or greater risk
- It emphasizes shared clinical decision-making in ambiguous cases and reiterates the critical role of HPV vaccination—while recognizing its reduced effectiveness in some immunocompromised populations

Surgical management

Marie Plante, Sven Mahner Alexandra Sebastianelli et al.

This exploratory analysis sought to evaluate outcomes based on surgical approach among patients who underwent simple hysterectomy

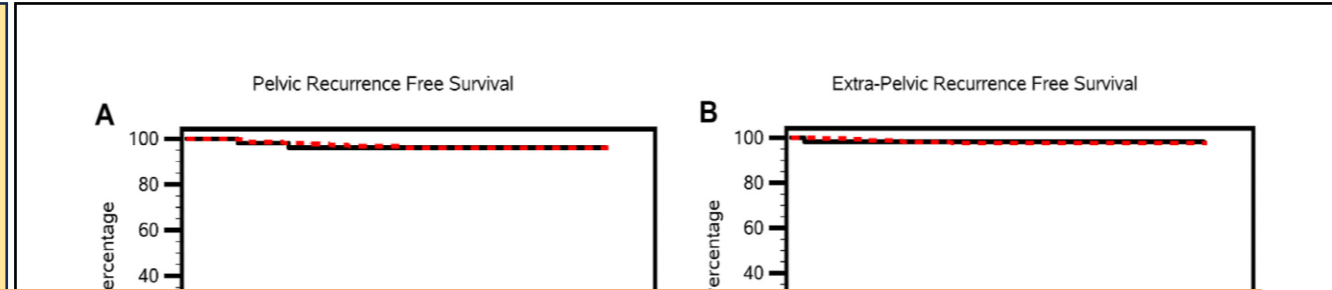
Objectives:

- To compare oncologic outcomes (RFS & OS) – MIS vs. open surgery in patients meeting SHAPE criteria
- To determine whether MIS is a safe alternative to open surgery in this low-risk population

- **Median Follow-up- 4.5 years**
- **Recurrence rates:**
 - ▶ MIS: 4.3% (12 recurrences)
 - ▶ Open: 5.3% (3 recurrences) → Not statistically significant ($p = 0.73$)
- **Survival:**
 - ▶ No significant differences in pelvic, extra-pelvic, or overall survival between MIS and open groups
 - ▶ All Cervical cancer-related deaths (4 total) occurred in MIS group, but numbers were too small to draw firm conclusions

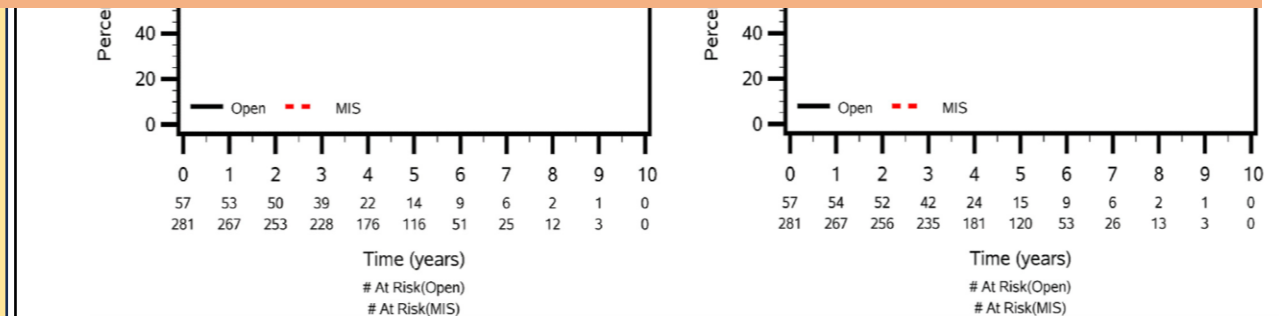
Results

A. 3-year pelvic RFS- 97.7% (95% CI 94.9-99.0) in MIS group vs 96.1% (95% CI 95.3-99.0) in open surgery



- **Adverse pathology findings** were similar across groups except:
 - ▶ MIS had **fewer cases of residual disease** (43.1% vs 57.9%, $p = 0.04$).
 - ▶ MIS had more adenocarcinoma histology and fewer adenosquamous cases
- **No statistically significant evidence** was found that MIS worsens clinical outcomes for patients with low-risk cervical cancer undergoing SH

D. Overall survival - 98.9% (95% CI 96.5-99.6) MIS vs 100% (95% CI 100-100) open group



- Factors associated with **worse outcomes**:
 - **Lymphovascular space invasion**
 - **Adjuvant treatment**
- The findings contrast with the **LACC trial**, which showed worse outcomes for MIS in **radical** hysterectomy, especially with tumors <2 cm.
- Results are reassuring but **caution is warranted**:
 - ▶ The study **was not powered or designed** to evaluate surgical approach impact
 - ▶ **Small no.** of recurrences observed

Conclusions

- **Minimally invasive simple hysterectomy** appears **safe** in patients meeting SHAPE criteria, **but evidence is not definitive**
- Further validation through **prospective trials** is necessary

Sentinel lymph node biopsy without systematic pelvic lymphadenectomy in females with early-stage cervical cancer: final outcome of the SENTIX prospective, single-arm, noninferiority, international trial

David Cibula, Simone Marnitz, Jiri Jarkovský et al

SENTIX trial prospectively evaluated the safety of SLN biopsy without PLND in early-stage cervical cancer

47 sites in 18 countries

Inclusion criteria

FIGO 2018 stage IA1/LVSI+ to IB2 disease

Exclusion criteria

Patients with undetected, unilateral or intraoperatively metastatic SLNs

Participants: 594 women with FIGO 2018 stages IA1 (with LVSI) to IB2

Intervention: SLN biopsy only + surgery (no PLND)

Primary Endpoint: 2-year recurrence rate
SLN assessed by pathological ultra staging

Results

- Median follow-up of 47 (range 1–76) months
- Disease recurrence - 54 patients
- Recurrence:
 - Localized in the pelvis in 25 patients (46%)
 - Localized at pelvic side wall- 4 (7%)
 - Extrapelvic site – 16 (30%)
- Median time to recurrence –
 - 19 (IQR 8–24)months- Pelvic
 - 16 (IQR 11–28)months - Extrapelvic
 - 14 (IQR 10–33) months -combined sites

Key results

1. SLN Detection:

- Bilateral SLN detection: 92.3%
- SLN metastases detected in 12% of patients:
 - 56.1% intraoperatively
 - 43.9% by ultrastaging

2. Recurrence:

- 2-year recurrence rate: 6.1% (noninferior to 7% benchmark)
 - Pelvic: 44.4%
 - Extrapelvic: 36.1%
 - Both: 19.4%

3. Survival (ITT Population):

- 2-year DFS: 93.3%
- 2-year Overall Survival: 97.9%

Risk Factors for Recurrence

- Tumor size >4 cm: HR = 5.23
- Presence of LVSI: HR = 2.65
- Tumor Grade 3: HR = 4.24
- Surgical approach (MIS vs open): Not significant (P = 0.509)

Clinical Implications

- SLN biopsy with ultrastaging:
 - Captured 44% of node-positive cases missed by standard methods
 - Reduces surgical morbidity (e.g., lymphoedema)
- Results support SLN biopsy as a staging method of choice for early-stage cervical cancer
- Findings challenge current guidelines still favoring PLND in most early-stage patients

Strengths & Limitations

Strengths:

- Large sample size (n=594, ITT)
- High bilateral SLN detection rate
- Comprehensive ultrastaging protocol
- Low dropout (1.5%)

Limitations:

- Non-randomized design
- Comparison with historical data for reference recurrence rate

Conclusion: SLN biopsy without PLND is a safe and effective alternative for staging early-stage cervical cancer, showing noninferior recurrence and survival outcomes, while offering reduced morbidity and better detection sensitivity for small metastases

Management of LACC

Neoadjuvant or concurrent atezolizumab with chemoradiation for locally advanced cervical cancer: a randomized phase I trial

Mayadev, J., Zamarin, D., Deng, W., et al.

- Combined immune checkpoint blockade (ICB) and chemoradiation (CRT) is approved in patients with LACC but optimal sequencing of CRT and ICB is unknown
- NRG-GY017 (NCT03738228) - randomized phase I trial of atezolizumab (anti-PD-L1) neoadjuvant and concurrent with CRT (Arm A) vs. concurrent with CRT (Arm B) in patients with high-risk node-positive LACC
- Primary endpoint - fraction of expanded tumor-associated T-cell receptor (TCR) clones in blood at day 21 as a surrogate measure of anti-tumor immune response
- Secondary objectives - safety and feasibility, 2-year DFS & predictive value of PD-L1 expression

Results

Primary Endpoint

- Tumor-associated TCR clonal expansion was significantly higher in Arm A (neoadjuvant) after 1 cycle of therapy ($p = 0.0025$), suggesting a more tumor-specific immune activation
- At day 21, the difference remained ($p = 0.052$ by t-test), although not statistically significant by Wilcoxon test ($p = 0.13$)
- Overall, neoadjuvant ICB initiated a more tumor-specific and systemic immune response before CRT blunted it (possibly due to lymphodepletion and T-cell killing in lymph nodes by radiation)

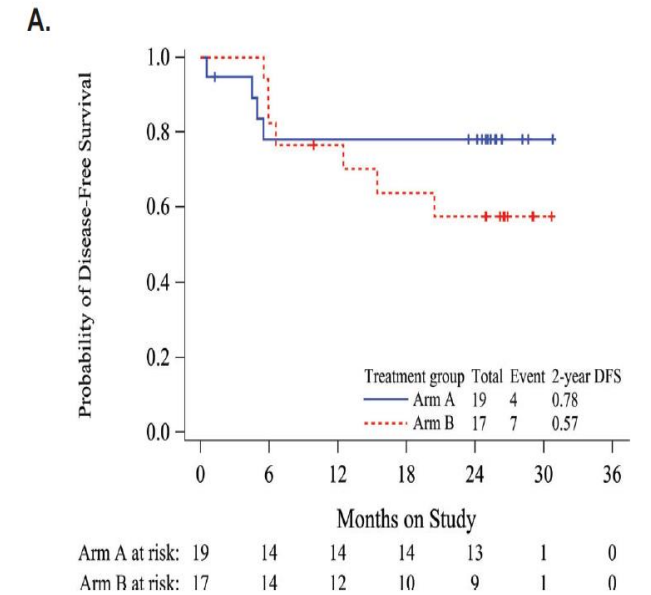
Secondary objectives

Safety

- Both arms showed acceptable safety profiles:
 - Arm A: No dose-limiting toxicities (DLTs)
 - Arm B: 3 DLTs (including immune-related colitis and cytopenias)
- 75% of all patients completed the full treatment regimen

Efficacy

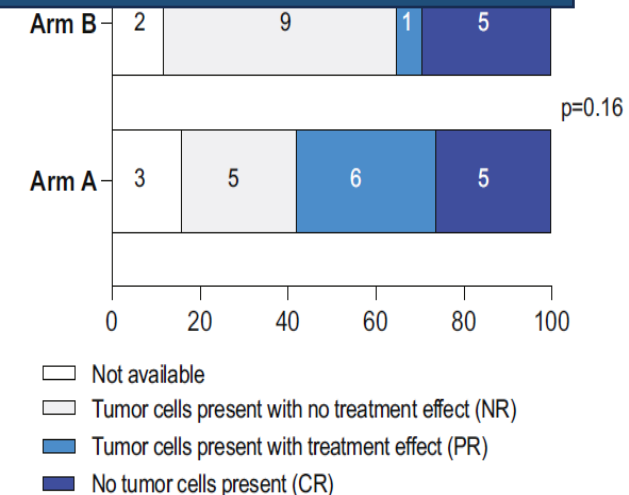
- 2-year disease-free survival (DFS):
 - 76% in Arm A vs. 56% in Arm B (*not statistically significant, $p = 0.28$*)
- Pathologic treatment effect observed in 69% of Arm A vs. 40% in Arm B
- Although not powered for efficacy, Arm A showed a favorable trend in DFS and tumor regression



A. Clinical outcomes. A Kaplan-Meier curve for

Conclusion- Neoadjuvant ICB prior to CRT was safe and was associated with immunologically and clinically favorable outcomes, warranting larger confirmatory studies

- ❖ However, a higher proportion of expanded clones were tumor associated in Arm A
- ❖ Higher total TCR expansion was negatively associated with 2-year DFS, likely due to non-specific inflammation rather than tumor-directed immunity
- ❖ PD-L1 expression (in tumors and immune cells) was not predictive of DFS or TCR expansion



Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial

Domenica Lorusso et al, *Lancet* 2024; 403: 1341–50

Study Design

Randomised, double-blind, placebo-controlled, phase 3 clinical trial

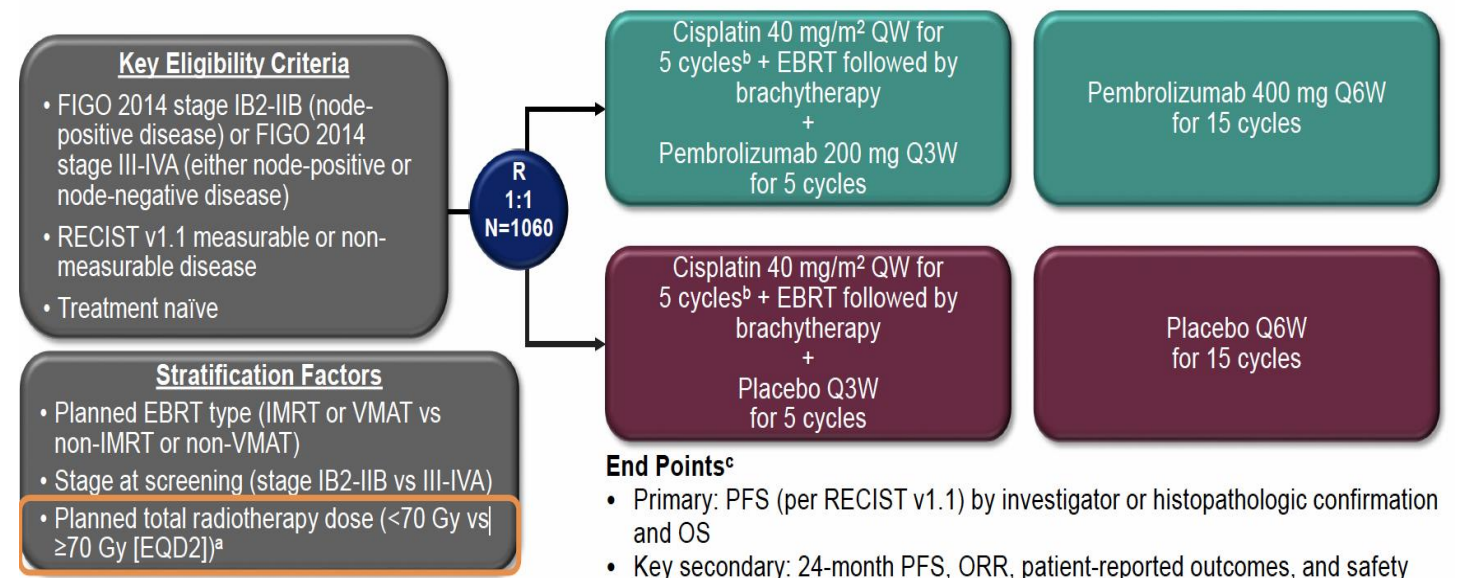
Study population

1060 patients

- ✓ 529- Pmb+CRT → 305 remained on t/t
- ✓ 531- Placebo+CRT → 209 remained on t/t

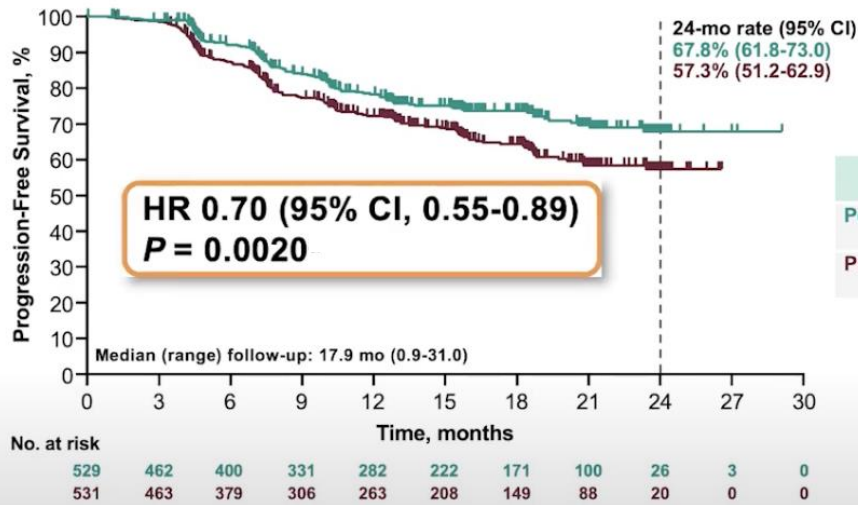
176 medical centres, 30 countries

Objective: To assess the efficacy and safety of adding pembrolizumab to chemoradiotherapy in locally advanced cervical cancer



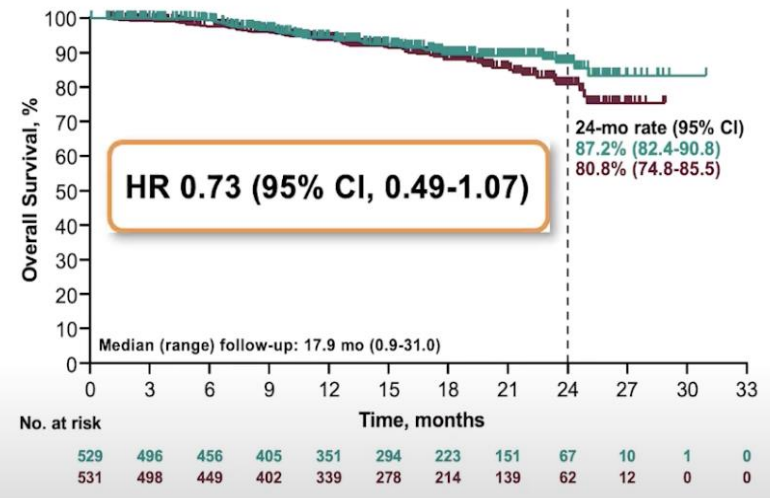
Results

Primary endpoint
Progression-free survival



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	21.7%	NR (NR-NR)
Placebo Arm	29.0%	NR (NR-NR)

Primary endpoint
Overall survival



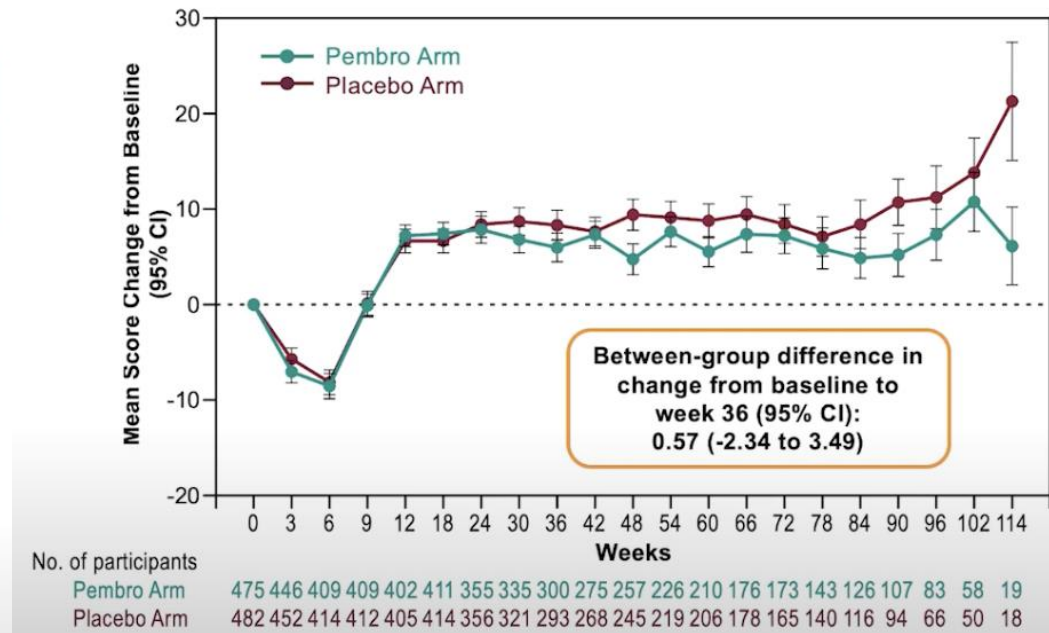
	Pts w/ Event*	Median, mo (95% CI)
Pembro Arm	8.3%	NR (NR-NR)
Placebo Arm	11.1%	NR (NR-NR)

*42.9% information fraction^a

Adverse events

	All-Cause AEs		Treatment-Related AEs ^a		Immune-Mediated AEs ^b	
	Pembro Arm (N = 528)	Placebo Arm (N = 530)	Pembro Arm (N = 528)	Placebo Arm (N = 530)	Pembro Arm (N = 528)	Placebo Arm (N = 530)
Any grade	525 (99.4%)	526 (99.2%)	507 (96.0%)	509 (96.0%)	172 (32.6%)	62 (11.7%)
Grade ≥3	394 (74.6%)	364 (68.7%)	354 (67.0%)	321 (60.6%)	22 (4.2%)	6 (1.1%)
Serious	150 (28.4%)	131 (24.7%)	91 (17.2%)	65 (12.3%)	15 (2.8%)	6 (1.1%)
Led to death	5 (0.9%)	6 (1.1%)	2 (0.4%) ^c	2 (0.4%) ^d	0	0
Led to discontinuation						
Any treatment	92 (17.4%)	75 (14.2%)	81 (15.3%)	67 (12.6%)	12 (2.3%)	2 (0.4%)
All treatment	1 (0.2%)	2 (0.4%)	0	1 (0.2%)	0	0

EORTC quality-of-life Core 30



Limitation of the study

The short duration of follow-up at this early timepoint, precluding the assessment of mature survival data; follow-up is ongoing and planned for future reporting

Conclusion

Early overall survival data are supportive of the PFS results, and the safety profile was as expected, with AE clinically manageable with dose adjustments and use of concomitant medications. Findings suggest a potential role for addition of pembrolizumab to chemoradiotherapy for treatment of newly diagnosed, high-risk, LACC.

Pembrolizumab with chemoradiotherapy in patients with high-risk locally advanced cervical cancer: Final analysis results of the phase 3, randomized, double-blind ENGOT-cx11/GOG-3047/KEYNOTE-A18 study

Linda R. Duska et al presented at ASCO 2025

Protocol-specified FA (Jan 7, 2025, data cutoff)

- Median follow-up was 41.9 mo (range, 24.8-55.0)
- 86 pts had received post-progression immunotherapy-

Summary of PFS and OS in ENGOT-cx11/GOG-3047/KEYNOTE-A18.						
	Final Analysis 07JAN25		Interim Analysis 2 08JAN24		Interim Analysis 1 09JAN23	
	Pembro + CCRT	Pbo + CCRT	Pembro + CCRT	Pbo + CCRT	Pembro + CCRT	Pbo + CCRT
OS, median (95% CI)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)
36-mo OS	81.8%	74.4%	82.6%	74.8%	NR (NR-NR)	NR (NR-NR)
HR (95% CI)	0.73 (0.57-0.94)		0.67 (0.50-0.90); P=0.0040		0.73 (0.49-1.07); P=0.0541	
PFS, median (95% CI)	47.6 (47.6-NR)	47.5 (41.0-NR)	NR (NR-NR)	NR (32.0-NR)	NR (NR-NR)	NR (NR-NR)
24-mo PFS	70.6%	59.7%	70.6%	58.6%	67.8%	57.3%
HR (95% CI)	0.72 (0.59-0.87)		0.68 (0.56-0.84)		0.70 (0.55-0.89)	

Conclusion

- With an additional 12 month median follow-up, pembro + CCRT continued to show clinically meaningful improvements in OS and PFS vs pbo + CCRT in pts with high-risk LACC and had a manageable safety profile
- These data are consistent with the prior interim analysis and provide further support for pembro + CCRT as the new standard of care for this population

2025

DOI: [10.1016/j.annonc.2025.05.533](https://doi.org/10.1016/j.annonc.2025.05.533)

ORIGINAL ARTICLE

Ultrasensitive detection and tracking of circulating tumor DNA to predict relapse and survival in patients with locally advanced cervical cancer: phase III CALLA trial analyses

J. Mayadev, J. C. Vázquez Limón, F. J. Ramírez Godínez et al.

AIM: To assess if adding durvalumab, a PD-L1 checkpoint inhibitor, could improve outcomes when combined with CRT

Further explored whether ultrasensitive detection of circulating tumor DNA (ctDNA) and circulating HPV DNA (cHPV DNA) could serve as predictive markers for relapse and survival

Phase III, randomized, double-blind, placebo-controlled trial

Enrolled 770 patients with FIGO 2009 stage IB2-IIB node-positive or IIIA-IVA any node-status untreated LACC

Randomized 1:1 to receive either:

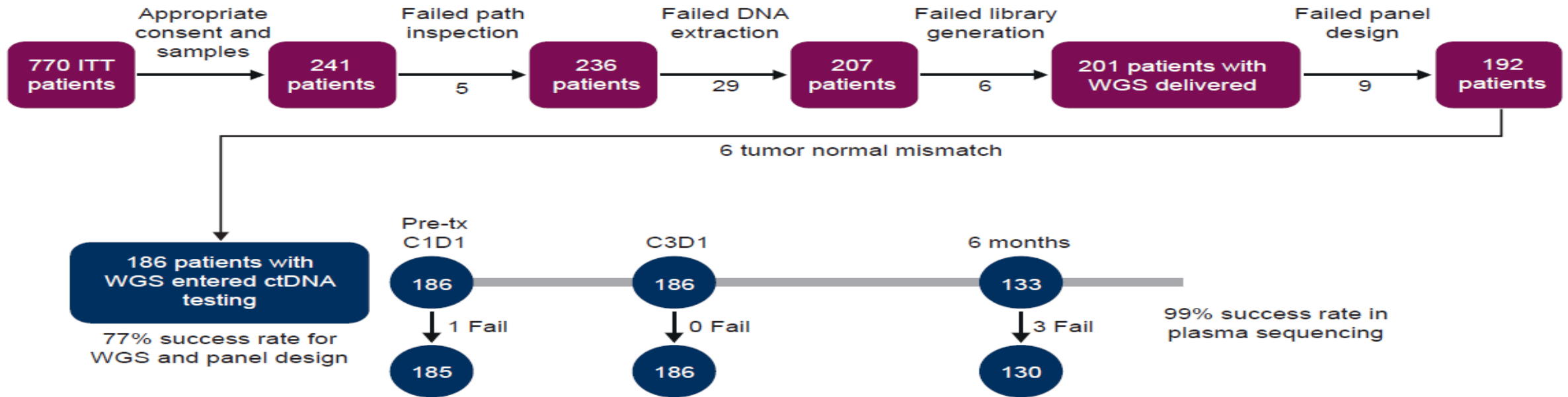
CRT + placebo

CRT + durvalumab

ctDNA and cHPV DNA were measured at:

- Baseline (before CRT)
- C3D1 (after CRT)
- C6D1 (3 months post-CRT)

Personalized whole genome sequencing-based tumor-informed NeXT Personal® assay used

A

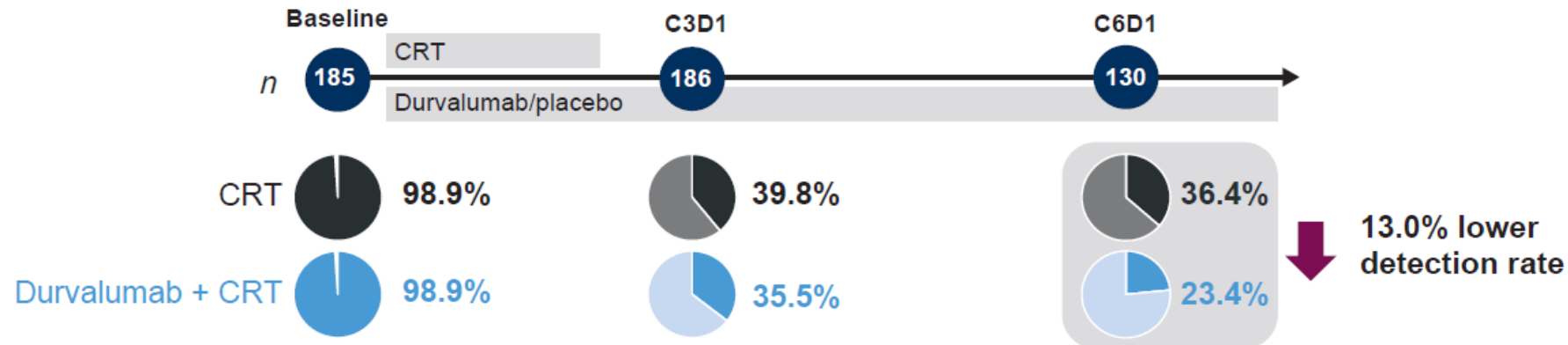
- 770 women were randomized in the CALLA study, 241 of whom provided informed consent for both germline and somatic genetic sequencing and had the appropriate samples collected
- BAP (Biomarker accessible population) 185 patients at baseline, 186 at C3D1, and 130 at C6D1
- 129 patients had evaluable samples at all time points

Key findings

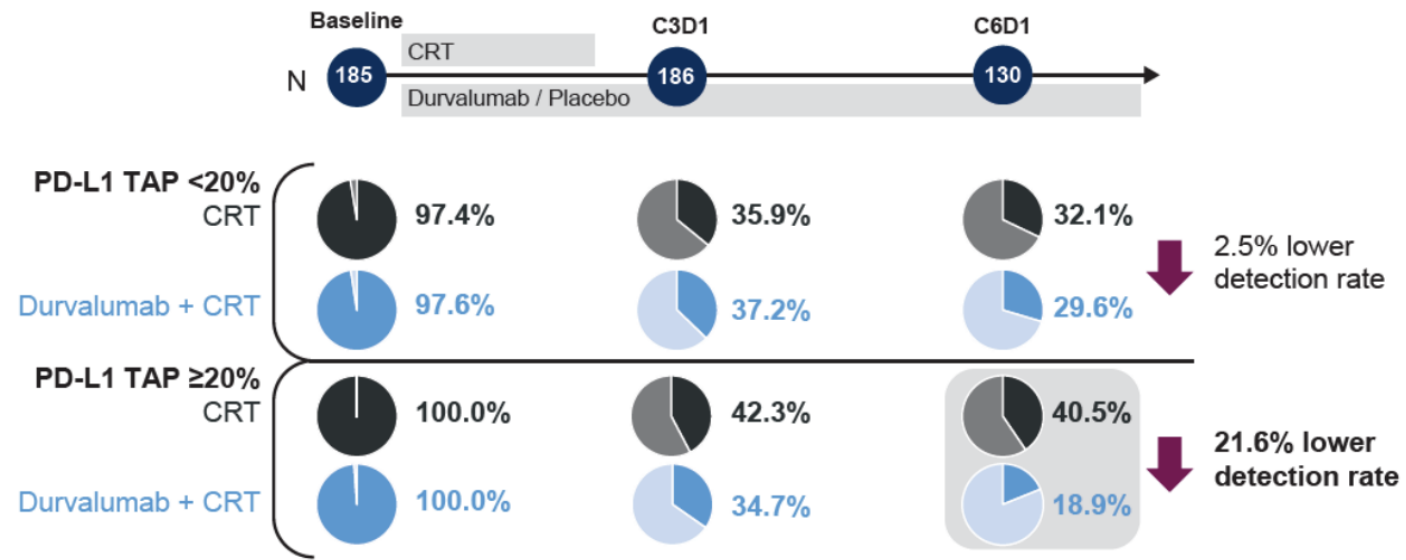
Detection of ctDNA and cHPV DNA before and during treatment

1. ctDNA Detection

- Detected in 98.9% of patients at baseline with no difference across the treatment arms



2. ctDNA detection rate in PD-L1 TAP <20% & PD-L1 TAP ≥20% subgroup



Key findings

cHPV DNA Detection

- Detection rate for cHPV DNA at baseline was similar to that for ctDNA [98.9% (91/92) for the durvalumab + CRT arm and 100% (91/91) for the CRT arm, but upon treatment, cHPV DNA detection did not decrease to the same extent as ctDNA
- Post-treatment cHPV DNA was less predictive than ctDNA

	CRT		Durvalumab + CRT	
	ctDNA	cHPV DNA	ctDNA	cHPV DNA
Baseline status				
Detected, <i>n</i> (%)	92 (98.9)	91 (100)	91 (98.9)	93 (98.9)
PPM, median [range]	4229.1 [0-56107.9]		6187 [0-244245.6]	
Viral copies/ml, median [range]		49.5 [0.00370-5030]		68.7 [0-10,300]
C3D1 status				
Detected, <i>n</i> (%)	37 (39.8)	71 (78)	33 (35.5)	84 (88.4)
PPM, median [range]	1.8 [0-96672.8]		1.7 [0-40906.2]	
Viral copies/ml, median [range]		0.0334 [0-466]		0.0241 [0-1650]
C6D1 status				
Detected, <i>n</i> (%)	24 (36.4)	41 (64.1)	15 (23.4)	45 (68.2)
PPM, median [range]	1.7 [0-17395.5]		0.9 [0-106957.4]	
Viral copies/ml, median, [range]		0.0117 [0-921]		0.0129 [0-1140]

Association of On-Treatment ctDNA and cHPV DNA with Clinical Outcomes

ctDNA detection after treatment (C3D1 & C6D1) was strongly associated with worse PFS & OS in both treatment groups (durvalumab + CRT and CRT alone)

- Patients with no detectable ctDNA at C3D1 had HRs 0.23 and at C6D1 HRs 0.04 - >90% reduction in risk of progression and death
- Persistent ctDNA predicted relapse a median of 5–5.5 months earlier than radiographic

Conclusion:

This study demonstrates the potential utility of ultrasensitive detection of ctDNA as a predictive and prognostic marker of disease progression and OS in LACC independent of disease stage

reduce this effect

Multivariate analysis confirmed:

- ctDNA is an independent prognostic marker of progression and survival.
- At C6D1, ctDNA was the only significant factor, outperforming cHPV DNA, treatment arm, and node status



Thank You!

A colorful brushstroke graphic in shades of blue, purple, pink, orange, and yellow, positioned below the 'Thank You!' text.