MRO . ART
MODERN RADIATION ONCOLOGY
35° RESIDENTIAL COURSE

MRO.35: Equity and Research in Oncology
26-27-28 OCTOBER 2025 - Fondazione Policlinico Universitario A. Gemelli IRCCS

Integrating **Checkpoint Inhibitors** with **Radiochemotherapy** in **L**ocally **A**dvanced **C**ervical **C**ancer: A New **Standard** for All Patients?

G. Macchia

gabriella.macchia@unicatt.it

Campobasso

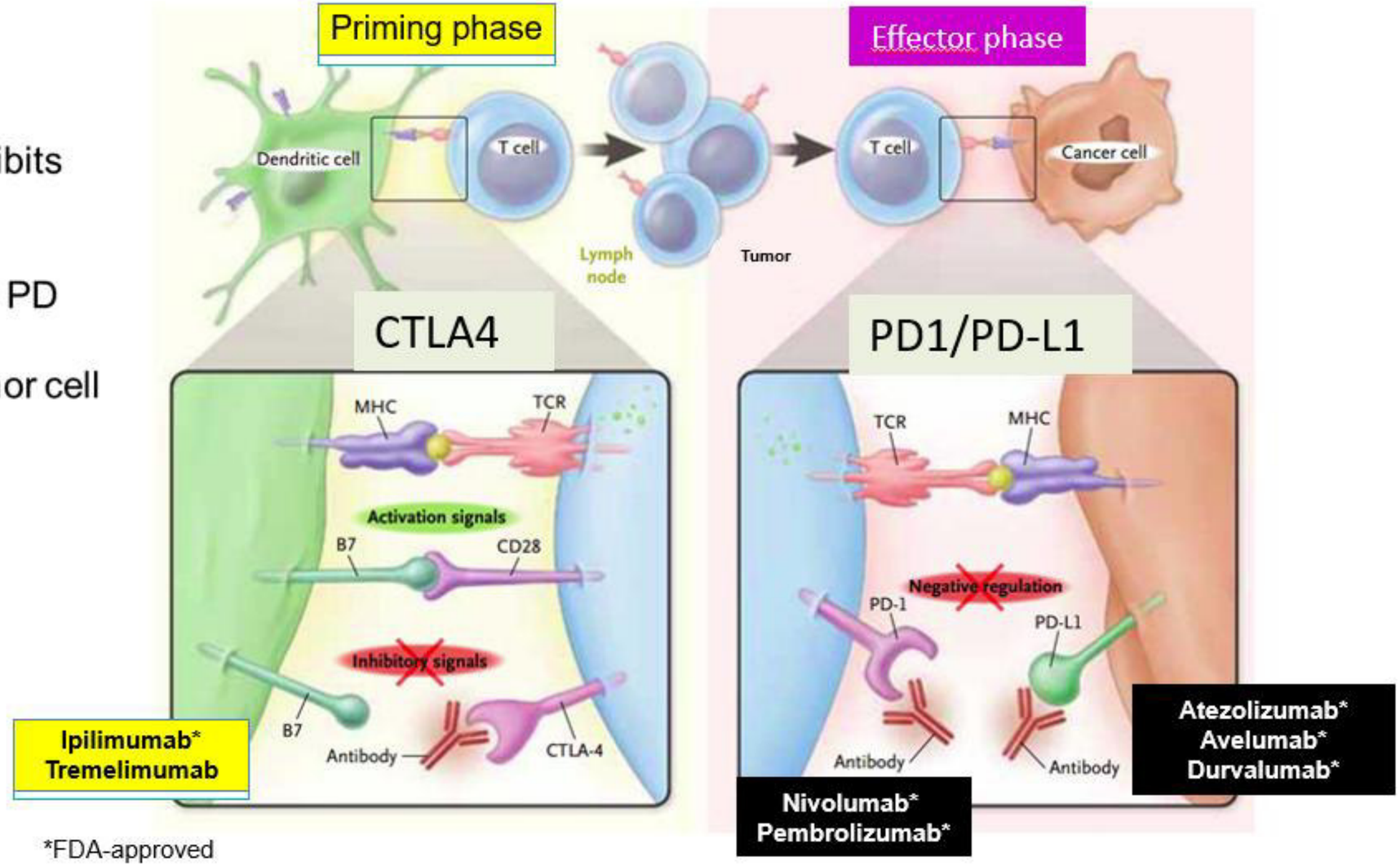
Gemelli
Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

GART
Advanced Radiation Therapy

Blockade of PD-1/PD-L1 and CTLA-4 Signaling in Tumor Immunotherapy

CTLA4 (cytotoxic T lymphocyte antigen 4) inhibits T cell activation

PD L1 (on tumor) binds to PD 1 (on effector T cell) and inhibits T cell killing of tumor cell

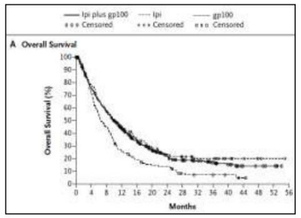


*FDA-approved

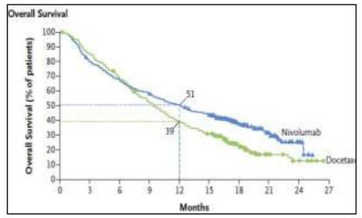
*FDA-approved

Adapted from Ribas A. *N Engl J Med*. 2012;366(26):2517-2519.

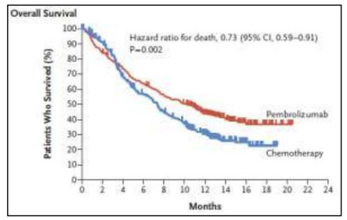
Immunotherapy improves Overall Survival in several diseases



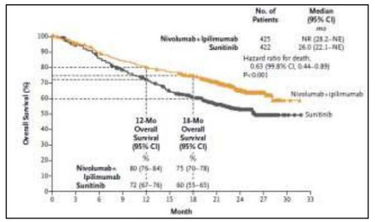
Metastatic Melanoma
Hodi NEJM 2010



Advanced NSCLC
Borghaei NEJM 2015



Advanced Urothelial Carcinoma
Bellmunt NEJM 2017

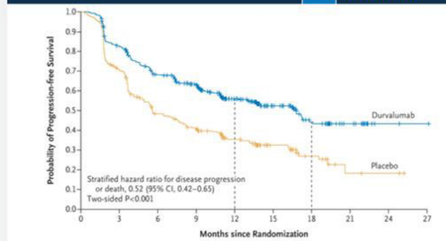


Advanced Renal Cell Carcinoma
Motzer NEJM 2018

15%-20% responders

PACIFIC: Phase III Trial of Durvalumab Post-CRT Maintenance for Locally-advanced, Unresectable NSCLC

Study Population	R	Arms	Efficacy Endpoints
• NSCLC Stage 3 Unresectable • Prior ≥2 cycles of platinum-based Tx with concurrent radiation • N= 713	2:1	→ Durvalumab 10 mg/kg IV Q2W up to 12 months Vs → Placebo	**Primary:** PFS, OS **Secondary:** 12 mo PFS, 18 mo PFS, 24 mo OS, ORR, DOR, Time to death, Time to distant metastasis



	Durvalumab	Placebo
No of Events/ No of Patients	214/476	157/237
PFS (95% CI)	16.8 (13-18.1)	5.6 (4.6-7.8)
OS (95% CI)	NR (34.7 –NR)	28.7 (22.9-NR)
12 mo PFS (95% CI)	55.9 (51-60.4)	35.3 (29-41.7)
18 mo PFS (95% CI)	44.2 (37.7-50.5)	27 (19.9-34.5)
24 mo OS (95% CI)	66.3 (61.7-70.4)	55.6 (48.9-61.8)

Antonia et al, NEJM 2017; Antonia et al, NEJM 2018

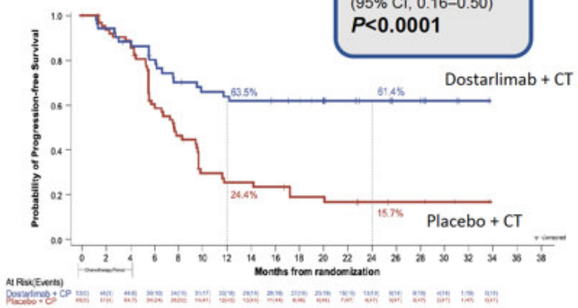
CONFIDENTIAL

GOG FOUNDATION

RUBY versus NRG-GY018 – progression-free survival

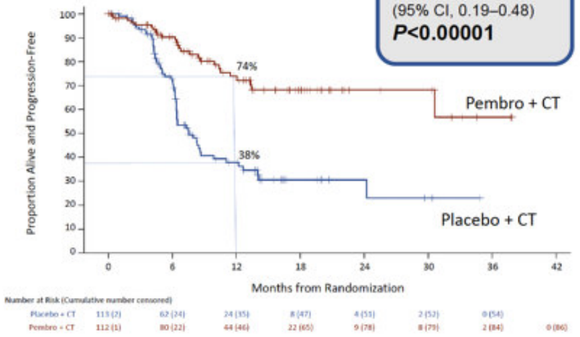
dMMR-MSI-H

HR, 0.28
(95% CI, 0.16–0.50)
***P*<0.0001**



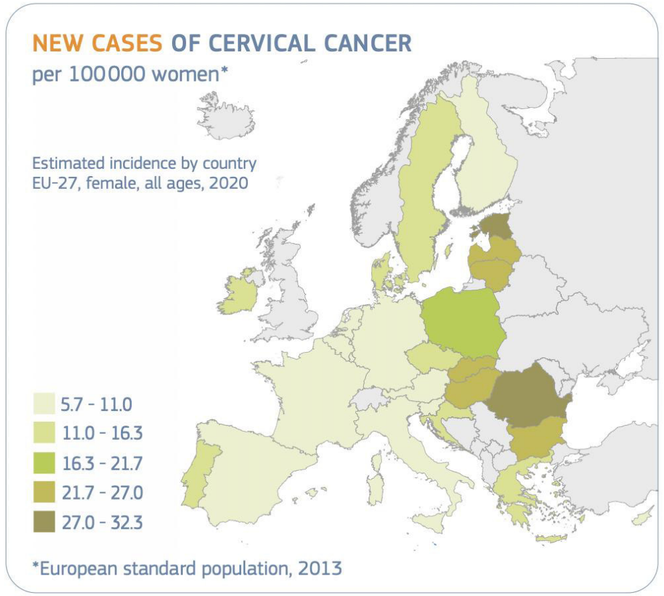
	No. with events, %	Median (95%CI), mo
Dostarlimab + CP	35.8	NR (11.8–NR)
Placebo + CP	72.3	7.7 (5.6–9.7)
PFS maturity	55.9	

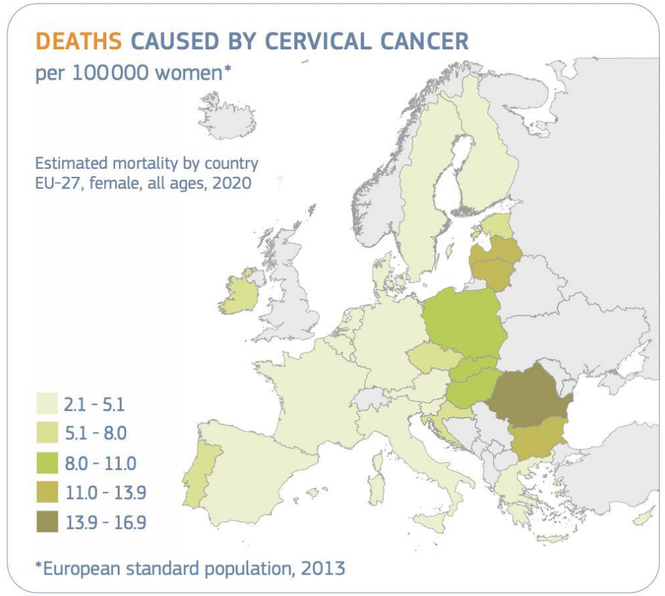
HR, 0.30
(95% CI, 0.19–0.48)
***P*<0.00001**



	No. with events, %	Median (95% CI), mo
Pembro + CT	23.2	NR (30.6–NR)
Placebo + CT	52.2	7.6 (6.4–9.9)
PFS maturity	37.7	

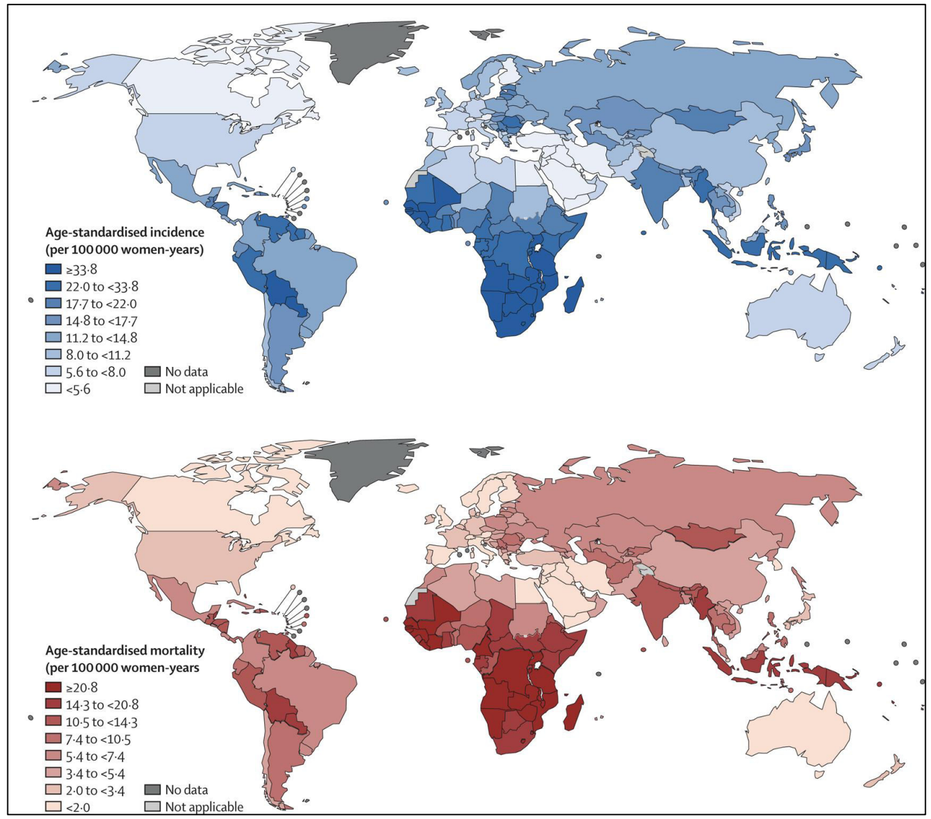
The Cervical Cancer Burden: Facts and Figures





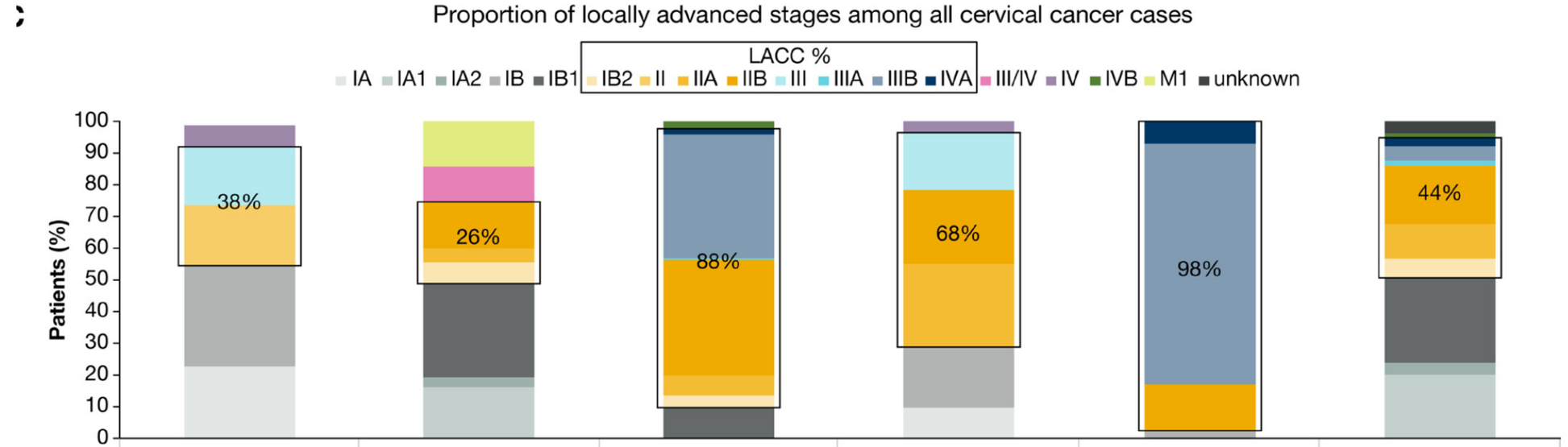
EU-27 2020
30,447 new cases
13,437 deaths

2020 Global Statistics
600,000 new cases
>300,000 deaths



Sung H et al. *CA Cancer J Clin*. 2021;71(3):209-249.

Proportions and Incidence of Locally Advanced Cervical Cancer (LACC)



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;32(12):1531-1539.

Evolution of Radiotherapy standard of care

Magnetic resonance imaging-based

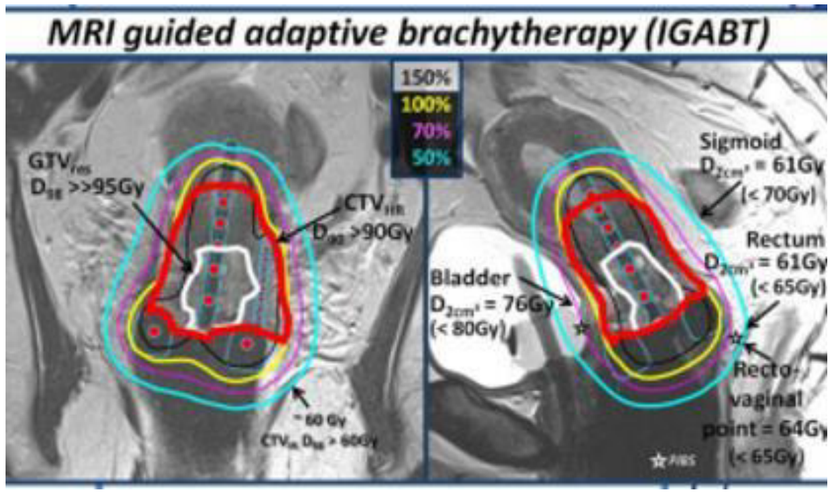
Image-guided Intensity-modulated EBRT

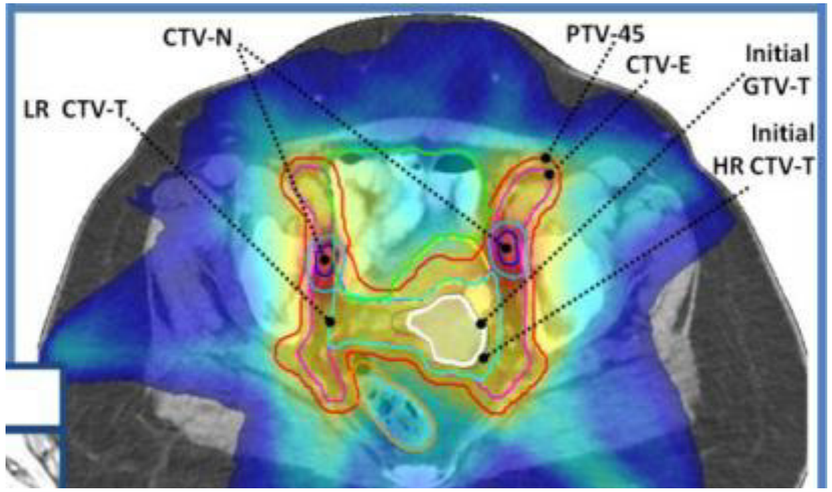
Image-guided adaptive brachytherapy

On-line Adaptive RT

Unprecedented local control rates of >90% across all stages

Improving pelvic control and survival rates by about 10% without increasing toxicity



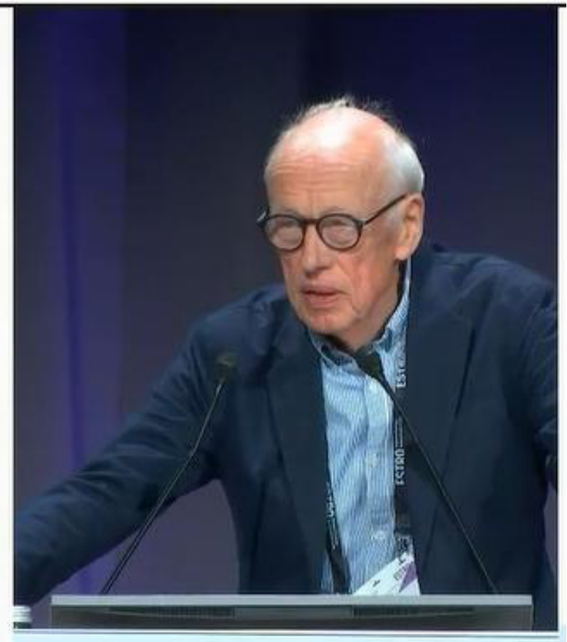


Schmid MP JCO 2023
Potter R Clin Transl Radiat Oncol 2018
Potter R Lancet Oncol 2021

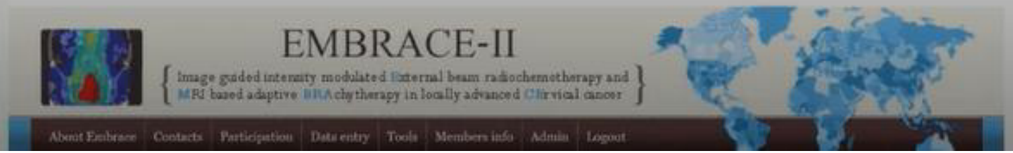
Richard Pötter, Kari Tanderup, Maximilian Schmid, Stefan Ecker, Petra Kroon, Jacob C. Lindegaard, Kjersti Bruheim, Barbara Segedin, Alina Sturdza, Henrike Westerveld, Supriya Chopra, Fleur Huang, Margit Valgma, Laura Velema, A.C. de Leeuw, Max Peters, Marianne Sanggaard-Assenholt, Nicole Eder- Nesvacil, Johannes Knoth, Monica Serban, Sofia Spampinato, Kathrin Kirchheiner, Remi Nout, Ina Jürgenliemk-Schulz, Christian Kirisits
EMBRACE Collaborative Group

EMBRACE II

A multicenter prospective interventional cohort study on IGRT-IMRT + cisplatin + MR-IGABT in locally advanced cervical cancer: overall results



Richard Pötter
Austria

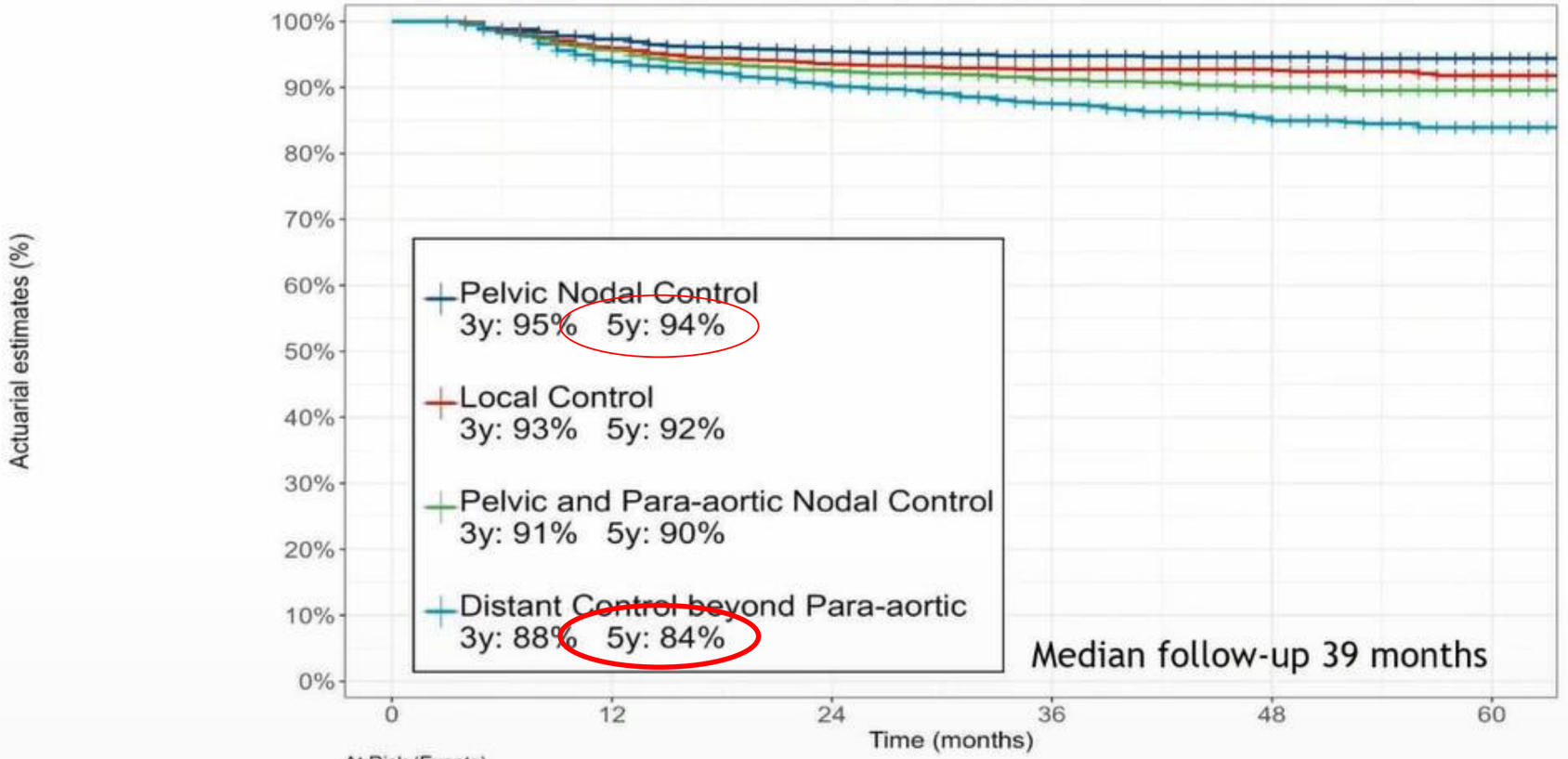


MEDICAL UNIVERSITY OF VIENNA

Control arm in the next studies!!!

Results: Disease control – overall cohort

(based on data from 11/2024)



At Risk (Events)						
Pelvic Nodal Control	1358 (0)	1187 (35)	1056 (57)	864 (64)	557 (65)	272 (66)
Local Control	1358 (0)	1187 (53)	1056 (82)	864 (90)	557 (91)	272 (94)
Pelvic and Para-aortic Nodal Control	1358 (0)	1187 (58)	1056 (95)	864 (109)	557 (117)	272 (119)
Distant Control beyond Para-aortic	1358 (0)	1187 (80)	1056 (125)	864 (154)	557 (173)	272 (177)

	EMBRACE I	EMBRACE II	
V43	2.4l	1.5l (-900 cm^3)	= local control
EBRT in PAN in N1	35%	50% (+15%)	= morbidity nodal control with PAN RT
Brachytherapy			
BT IC/IS	43%	74% (+31%)	
CTV-HR D90	90Gy	92Gy (+2Gy)	= main local control = morbidity (although > Gy)
D2cc Rectum D2cc bowel	62Gy 63Gy	58Gy (-4Gy) 58Gy (-5Gy)	
PIBS		-15Gy	vaginal morbidity

1. Are all centers across Europe, or across Italy, **able to provide "EMBRACE style" radiotherapy**?

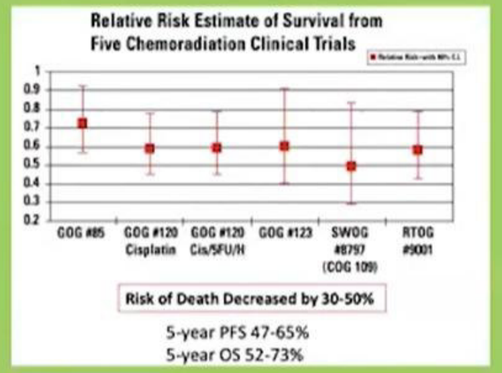
2. **What drug** can enhance the effect of **modern radiotherapy**?

3. Or maybe those who claim that **systemic therapies** can **compensate for inadequate radiotherapy** aren't entirely wrong.

LACC: Evolution of treatment

1999 | 2008-2015 | 2018-2020 | 2023-2025

CRT



Risk of death decreased by 30-50%

Meta-analysis:
OS HR: 0,81; 6% 5yOS
DFS HR: 0,78; 8% 5yDFS

NACT + surgery vs CRT
Gupta (N=633)

NACT + surgery vs CRT
EORTC-55994 (N=626)

CRT + adjuvant CT
OUTBACK trial (N=919)

IGBT with MRI/CT guide

RETROEMBRACE (N=731)
EMBRACE I (N=1341)

CRT + Anti-PDL1
CALLA (N=770)

CRT + Anti-PDLI
ATEZOLACC
(N=189)

CRT + Anti -PD1
KN A-18 (N=980)

Induction CT
followed by CRT
INTERLACE
(N=500)

EMBRACE II (N=1376)

After 25 years: Evolving Standard of Care

Immunotherapy in Cervical Cancer: Rationale

1.Cervical Cancer is a Virally Driven Cancer:

- Almost all cases are driven by HPV infection. The virus has evolved many ways of evading the immune system

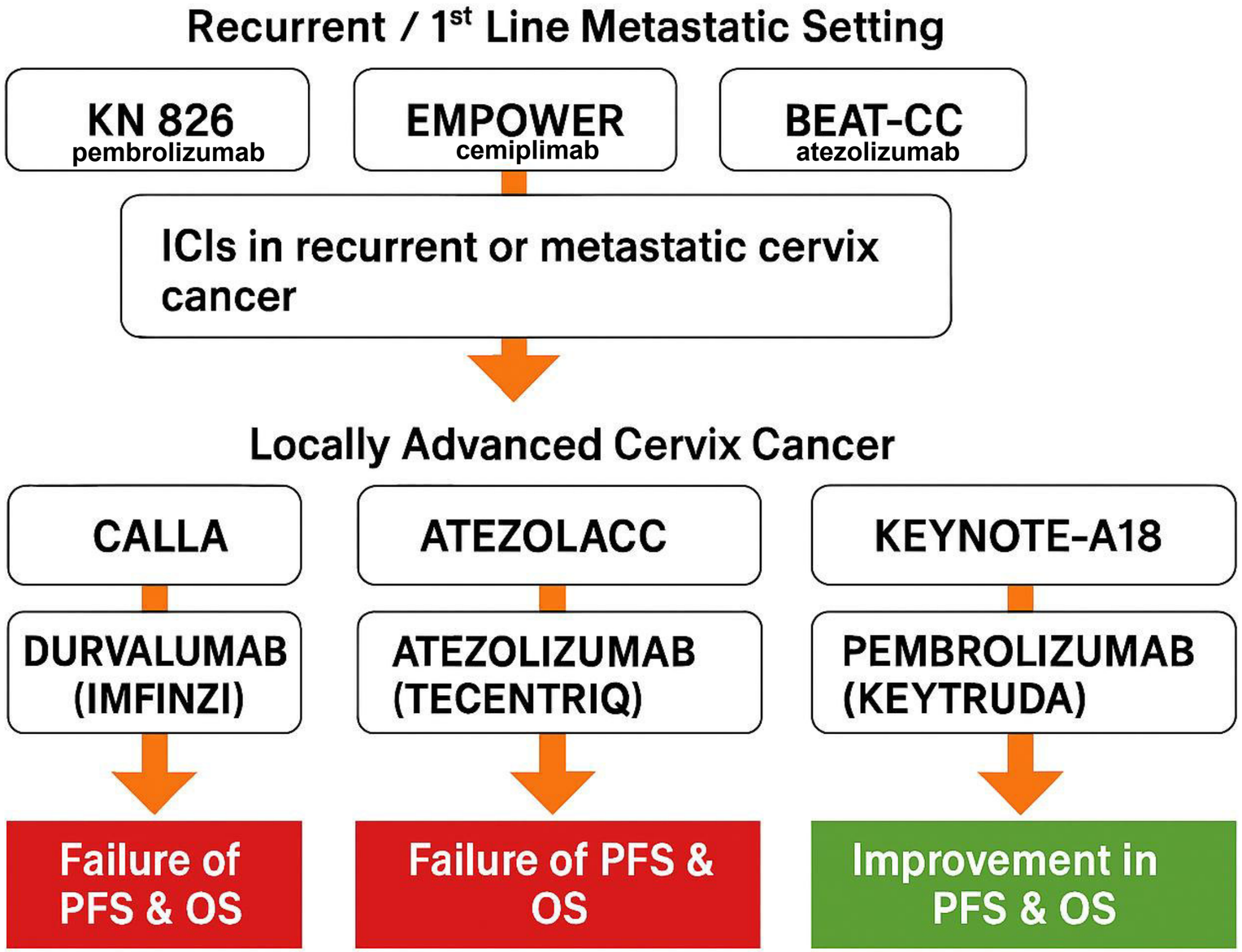
2. Immune-Privilege State: PD-L1 expression and Tumour Infiltrating Lymphocytes(TILs)

- PD-L1 is not expressed in normal cervical tissue, but is overexpressed in SCC(19% to 88%) and Adenocarcinoma(14%)
- The tumour microenvironment(the composition of) has an impact on survival rates:
  - Patients w negative LN have higher numbers of intraepithelial CD8+ cells than positive LN patients

3. Cervical Cancers Have an Increased Tumor Mutational Burden (TMB) Rate

- The rate of TMB in cervical cancers is about 5-6 mutations per megabase (behind melanoma, lung, bladder, oesophageal and colorectal cancers)
- Increased TMB lead to the presence of more neoantigens that then stimulate the immune system.

Smola, S, et al. *Ther Adv Vaccines.* 2017;5(3):69-82.Dyer et al JNCCN; Volume 17 Number 1 January 2019
S.J. Otter et al. / Clinical Oncology 31 (2019) 834e843; J. Otter et al. / Clinical Oncology 31 (2019) 834e843; Piersma SJ et al; Cancer Res 2007; 67: (1). January 1, 2007Alexandrov LB et al Nature 2013;500:415e421; S.J. Otter et al. Clinical Oncology 31 (2019) 834e843


Recurrent / 1st Line Metastatic Setting
KN 826
pembrolizumab
EMPOWER
cemiplimab
BEAT-CC
atezolizumab
ICIs in recurrent or metastatic cervix cancer
Locally Advanced Cervix Cancer
CALLA
ATEZOLACC
KEYNOTE-A18
DURVALUMAB (IMFINZI)
ATEZOLIZUMAB (TECENTRIQ)
PEMBROLIZUMAB (KEYTRUDA)
Failure of PFS & OS
Failure of PFS & OS
Improvement in PFS & OS

CALLA Study Design

15 countries, **120** sites

Eligible population

- Women aged ≥18 years
- Histologically confirmed cervical adenocarcinoma, squamous carcinoma, or adenosquamous carcinoma
- High-risk LACC (FIGO 2009)
  - Stages IB2 to IIB, node positive (N≥1)
  - Stages IIIA to IVA with any node (N≥0)
- WHO ECOG performance status of 0 or 1

Stratification factors

- Disease stage
  - FIGO Stage IB2–IIB and LN+
  - FIGO Stage ≥III and LN−
  - FIGO Stage ≥III and LN+
- Region of world

N=770

R 1:1

Durvalumab 1500 mg q4w × 24 doses
Platinum + EBRT + brachytherapy

Placebo q4w × 24 doses
Platinum + EBRT + brachytherapy

Primary Endpoint:

Progression-Free Survival[a] (Investigator-assessed)

Key Secondary Endpoints:

- Overall survival
- Objective response rate
- Duration of response
- Incidence of local or distant progression / 2° malignancy
- Safety and tolerability

Chemoradiotherapy Regimen

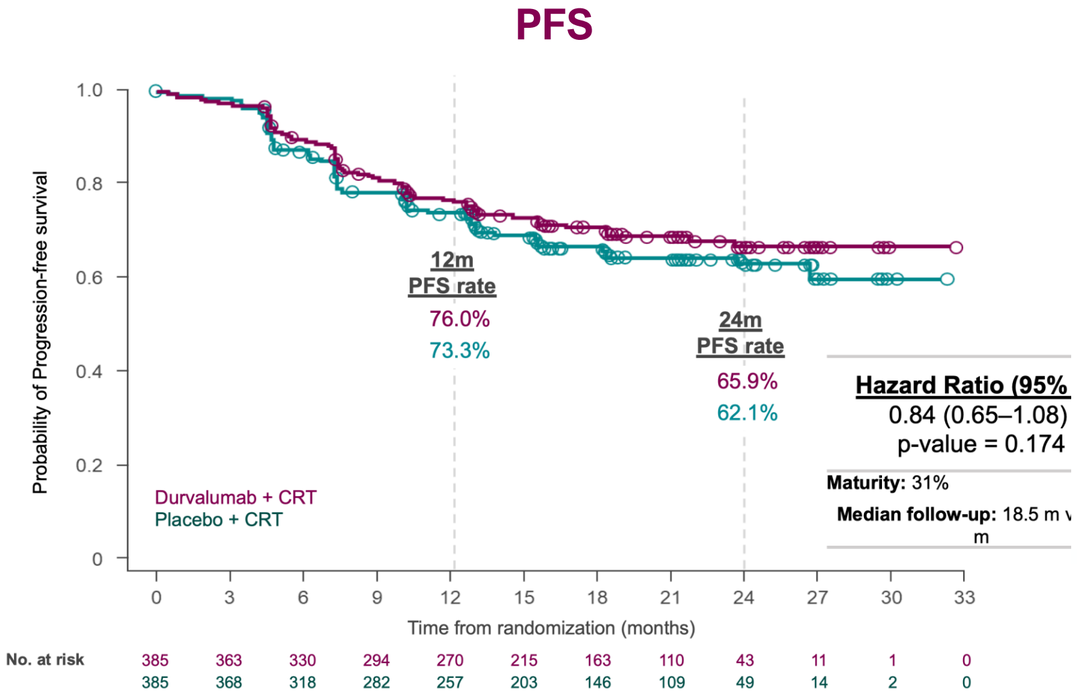
Platinum agent	Cisplatin 40 mg/m^2 or carboplatin AUC2 q1w × 5 weeks
EBRT	45 Gy in 25 fractions at 1.8 Gy/fraction, 5 fractions per week
Brachytherapy	High-dose rate: 27.5–30 Gy; Low/pulsed-dose rate: 35–40 Gy

Key Milestones

First patient in	February 2019
Last patient in	December 2020
Data cut off	January 20, 2022

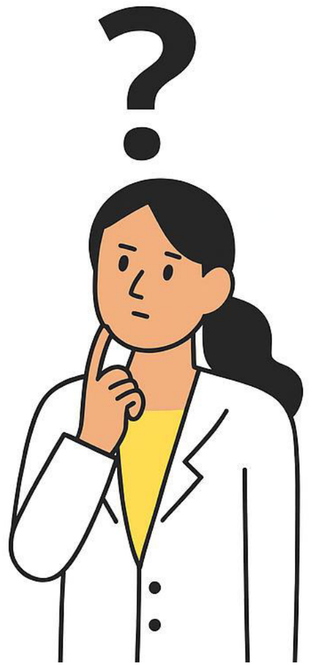
[a]According to RECIST 1.1 or histopathologic confirmation of local tumor progression using CT or MRI scans.

Progression-Free and Overall Survival



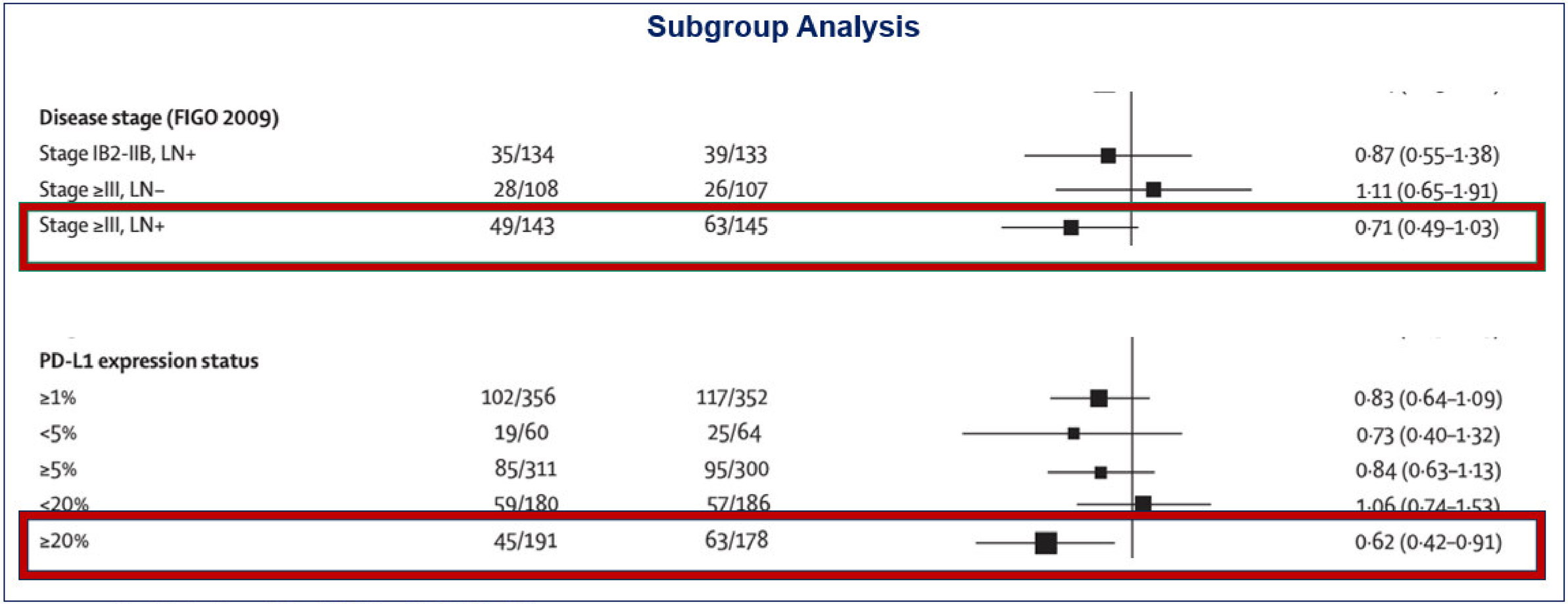
Why did the strategy fail?

- Was the checkpoint inhibitor administered concurrently with radiotherapy, potentially limiting its immunogenic synergy?
- Was the choice of checkpoint inhibitor suboptimal for this tumor type or setting?
- Low risk population reducing the likelihood of observing a meaningful benefit?



Locally-advanced CC Management:
Chemoradiation + anti-PDL1: CALLA trial

Subgroup Analysis



Disease stage (FIGO 2009)			
Stage IB2-IIB, LN+	35/134	39/133	0·87 (0·55–1·38)
Stage ≥III, LN–	28/108	26/107	1·11 (0·65–1·91)
Stage ≥III, LN+	49/143	63/145	0·71 (0·49–1·03)
PD-L1 expression status			
≥1%	102/356	117/352	0·83 (0·64–1·09)
<5%	19/60	25/64	0·73 (0·40–1·32)
≥5%	85/311	95/300	0·84 (0·63–1·13)
<20%	59/180	57/186	1·06 (0·74–1·53)
≥20%	45/191	63/178	0·62 (0·42–0·91)

Monk B. et al, Lancet Oncol 2023 Dec;24(12):1334-1348

ATEZOLACC: Randomized, open, phase II trial

Key Eligibility Criteria

(FIGO 2009) stage IB1-IIA and N+
or IIB-IVa
or IVb (metastases limited to para-aortic area) *

Stratification factors

FIGO 2009 IB-IIB vs IIIa-IVa vs Ivb
Pelvic nodal status (N+ vs N-)
Age (<50y vs ≥ 50 y)
Histology: SCC vs other

R
1:1
N = 189

EBRT 45 Gy IMRT / VMAT
Concurrent cisplatin 40 mg/m² QW
IGABT boost

EBRT 45 Gy IMRT
Concurrent cisplatin 40 mg/m² QW
IGABT boost

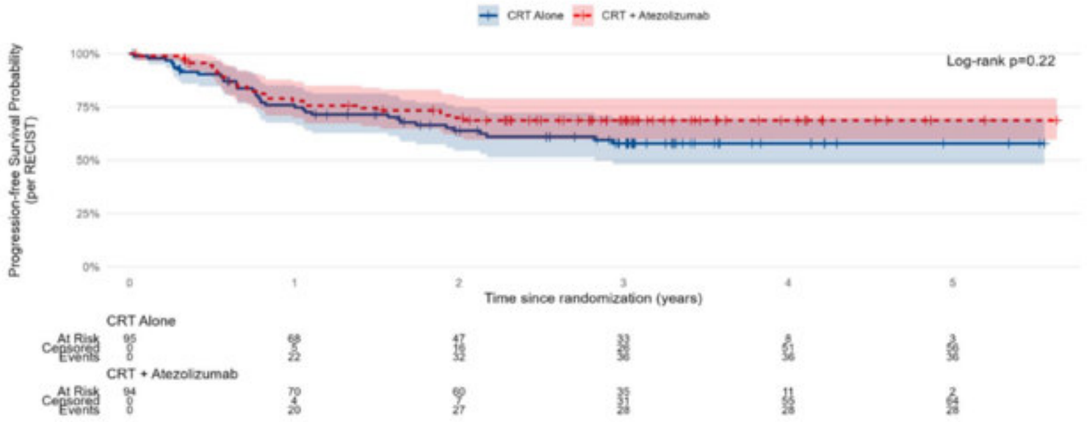
+ Atezolizumab 1200 mg IV every three weeks

Atezolizumab 1200 mg
IV /3 weeks
up to 20 cycles

*based on PET/CT

Primary endpoint: 2-y PFS

2-y PFS (95%CI)	
Standard arm	64% [55%; 75%]
Atezo arm	70% [61%; 80%]



HR (95%CI)
0.77 [0.46; 1.29]

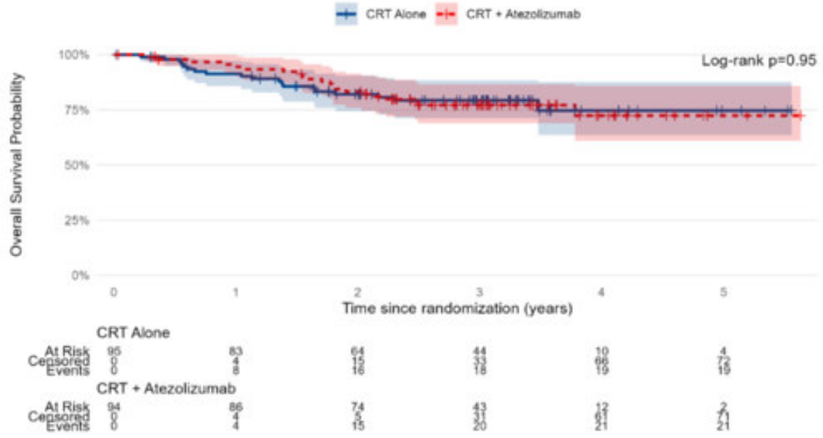
Why did the strategy fail?

- Was the checkpoint inhibitor administered concurrently with radiotherapy, potentially limiting its immunogenic synergy?
- Was the choice of checkpoint inhibitor suboptimal for this tumor type or setting?
- Low risk population reducing the likelihood of observing a meaningful benefit?

Secondary endpoints

2-y OS (95%CI)	
Standard arm	82% [74%; 90%]
Atezo arm	83% [76%; 91%]

Overall survival



HR (95%CI)
1.01 [0.52; 1.96]

ENGOT-cx11/GOG-3047/KEYNOTE-A18: Randomized, Double-Blind, Phase 3 Study

Key Eligibility Criteria

- FIGO 2014 stage IB2-IIB (node-positive disease) or FIGO 2014 stage III-IVA (either node-positive or node-negative disease)
- RECIST 1.1 measurable or non-measurable disease
- Treatment naïve

Stratification Factors

- Planned EBRT type (IMRT or VMAT vs non-IMRT or non-VMAT)
- Stage at screening (stage IB2-IIB N+ vs III-IVA)
- Planned total radiotherapy dose (<70 Gy vs ≥70 Gy [EQD2])

R
1:1
N = 1060

Cisplatin 40 mg/m^2 QW for 5 cycles[a] + EBRT followed by brachytherapy + Pembrolizumab 200 mg Q3W for 5 cycles	Pembrolizumab 400 mg Q6W for 15 cycles
Cisplatin 40 mg/m^2 QW for 5 cycles[a] + EBRT followed by brachytherapy + Placebo Q3W for 5 cycles	Placebo Q6W for 15 cycles

[a]A 6th cycle was allowed per investigator discretion. ENGOT-cx11/GOG-3047/KEYNOTE-A18 ClinicalTrials.gov identifier, NCT04221945.

Lorusso et al. Lancet 2024

Baseline Characteristics

	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Age, median (range), years	49 (22–87)	50 (22–78)
Race[a]		
White	254 (48.0)	264 (49.7)
Asian	155 (29.3)	148 (27.9)
Multiple	78 (14.7)	86 (16.2)
American Indian or Alaska Native	24 (4.5)	22 (4.1)
Black or African American	14 (2.6)	8 (1.5)
Native Hawaiian or Other Pacific Islander	2 (0.4)	1 (0.2)
PD-L1 CPS		
<1	22 (4.2)	28 (5.3)
≥1	502 (94.9)	498 (93.8)
Missing	5 (0.9)	5 (0.9)
ECOG PS 1	149 (28.2)	134 (25.2)
Squamous cell carcinoma	433 (81.9)	451 (84.9)

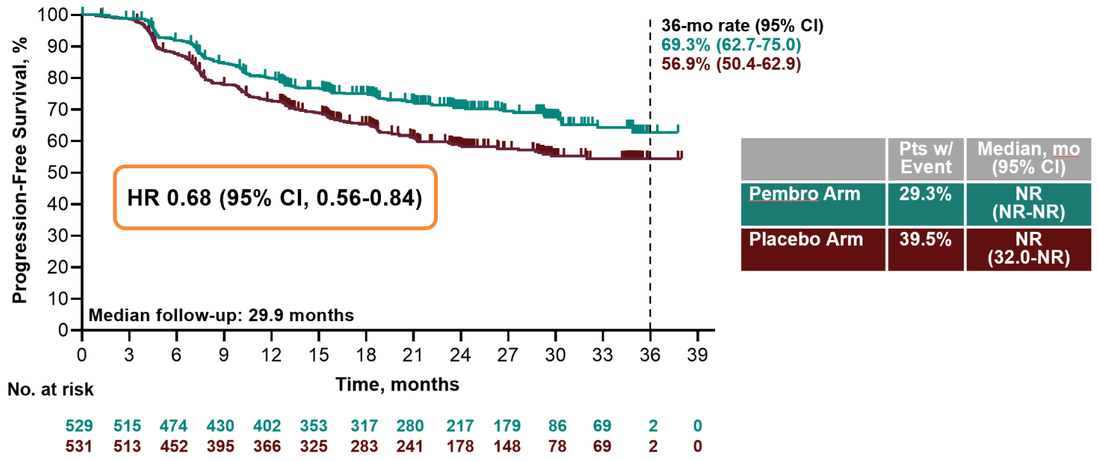
	Pembro Arm (N = 529)	Placebo Arm (N = 531)
Stage at screening (FIGO 2014 criteria)		
IB2-IIB	235 (44.4)	227 (42.7)
III-IVA	294 (55.6)	304 (57.3)
Lymph node involvement[b]		
Positive pelvic only	326 (61.6)	324 (61.0)
Positive para-aortic only	14 (2.6)	10 (1.9)
Positive pelvic and para-aortic	105 (19.8)	104 (19.6)
No positive pelvic or para-aortic	84 (15.9)	93 (17.5)
Planned type of EBRT		
IMRT or VMAT	469 (88.7)	470 (88.5)
Non-IMRT and non-VMAT	60 (11.3)	61 (11.5)
Planned total radiotherapy dose		
<70 Gy	47 (8.9)	46 (8.7)
≥70 Gy	482 (91.1)	485 (91.3)

Data are n (%) unless otherwise noted.
[a]In each treatment arm, 2 patients (0.4%) had missing information for race. [b]Per protocol, a positive lymph node was defined as ≥1.5 cm shortest dimension by MRI or CT.
Data cutoff date: January 9, 2023.

KEYNOTE-A18 strengths

- Randomized phase-III double-blind placebo-controlled design
- High-risk LACC population
- Short accrual period
- The majority treated with modern radiotherapy approach
- Good adherence to protocol-specified treatment
- 10.5% PFS benefit at 2-years
- Patient-reported HRQoL changes similar to the placebo arm

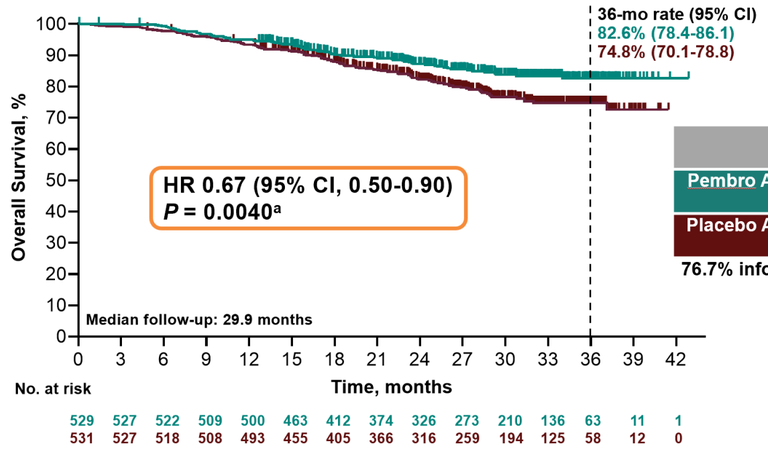
Updated Progression-Free Survival at IA2



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	29.3%	NR (NR-NR)
Placebo Arm	39.5%	NR (32.0-NR)

Lorusso D et al. *Lancet*. 2024;403:1341-50; Lorusso D et al.Lancet. 2024 Oct 5;404(10460):1321-1332

Primary Endpoint: Overall Survival at IA2



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	14.2%	NR (NR-NR)
Placebo Arm	20.5%	NR (NR-NR)

76.7% information fraction[a]

[a]With 184 of the 240 deaths expected at the final analysis (76.7% information fraction), the observed *P* = 0.0040 (1-sided) crossed the prespecified nominal boundary of 0·01026 (1-sided) at this planned second interim analysis. At this time, 66 patients had received immunotherapy as post-progression treatment, including 15/138 patients (10.9%) in the pembro arm and 51/193 patients (26.4%) in the placebo arm; of those, 10 (7.2%) and 41 (21.2%), respectively, had received pembro. Data cutoff date: January 8, 2024.

Lorusso D et al. *Lancet*. 2024;403:1341-50; Lorusso D et al.Lancet. 2024 Oct 5;404(10460):1321-1332

Why some trials with so strong biological rationale failed and other won?

Is it a matter of **strategy**?

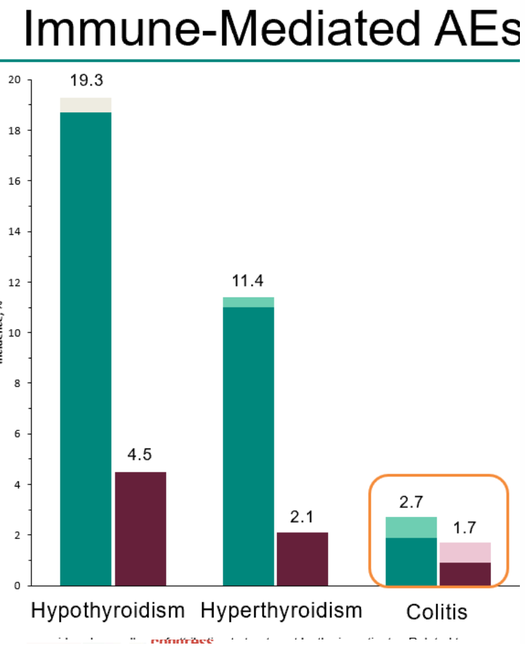
Or a matter of **trial**?

CALLA vs KEYNOTE-A18

Key Differences of studies	CALLA	KN-A18
Primary Endpoint	PFS	PFS/OS
Recruitment	N=770	N=980
Chemo for CRT	Either cisplatin or carboplatin	Cisplatin only
Study Treatment	Durvalumab 1500 mg IV every 4 weeks for 24 cycles	Pembrolizumab 200 mg Q3W (5 cycles) 400 mg Q6W (15 cycles)
Lymph Node Size and number	1 positive pelvic LFN required Amendment : Downsized LN size in short axis for CT (from 1.5 cm to 1 cm)	2 positive pelvic LFNs required Remained unchanged for LN size per RECIST 1.1 (≥1.5 cm shortest dimension)

- Real life versus clinical trial

BUT… we don't still have **Real life data**

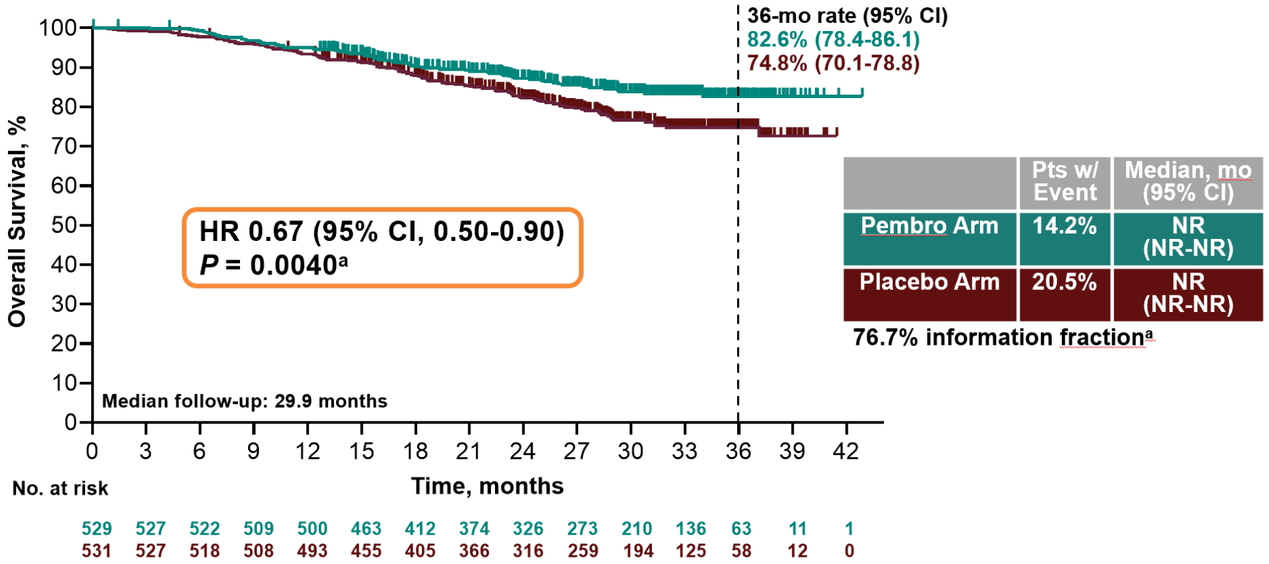


Clinical trials

Real life patients

- How long should maintenance be continued?

Primary Endpoint: Overall Survival at IA2



	Pts w/ Event	Median, mo (95% CI)
Pembro Arm	14.2%	NR (NR-NR)
Placebo Arm	20.5%	NR (NR-NR)

76.7% information fraction[a]

[a]With 184 of the 240 deaths expected at the final analysis (76.7% information fraction), the observed *P* = 0.0040 (1-sided) crossed the prespecified nominal boundary of 0·01026 (1-sided) at this planned second interim analysis. At this time, 66 patients had received immunotherapy as post-progression treatment, including 15/138 patients (10.9%) in the pembro arm and 51/193 patients (26.4%) in the placebo arm; of those, 10 (7.2%) and 41 (21.2%), respectively, had received pembro. Data cutoff date: January 8, 2024.

Lorusso D et al. *Lancet*. 2024;403:1341-50; Lorusso D et al.Lancet. 2024 Oct 5;404(10460):1321-1332

KN A18: Early splitting of PFS/OS curves: what is optimal duration of Pembrolizumab after CRT?

- Costs

💊 Pembrolizumab Cost Estimate (Italy – KN A18 Regimen)

Drug Requirement

- **Total dose**: 7,000 mg
  (5 cycles × 200 mg + 15 cycles × 400 mg)

Ex-Factory Price (Theoretical)

- **€37.98/mg**
- **Raw cost (no discount):**

$$7,000 \times €37.98 = €265,860.00$$

📉 Discount Scenarios (Typical in Oncology Settings)

Discount Applied	Estimated Actual Cost
30%	€186,102
50%	€132,930

📌 Final Estimate

Pembrolizumab "drugs only" cost in Italy (KN A18):

👉 **€130,000 – €190,000**

(Depending on negotiated discount)

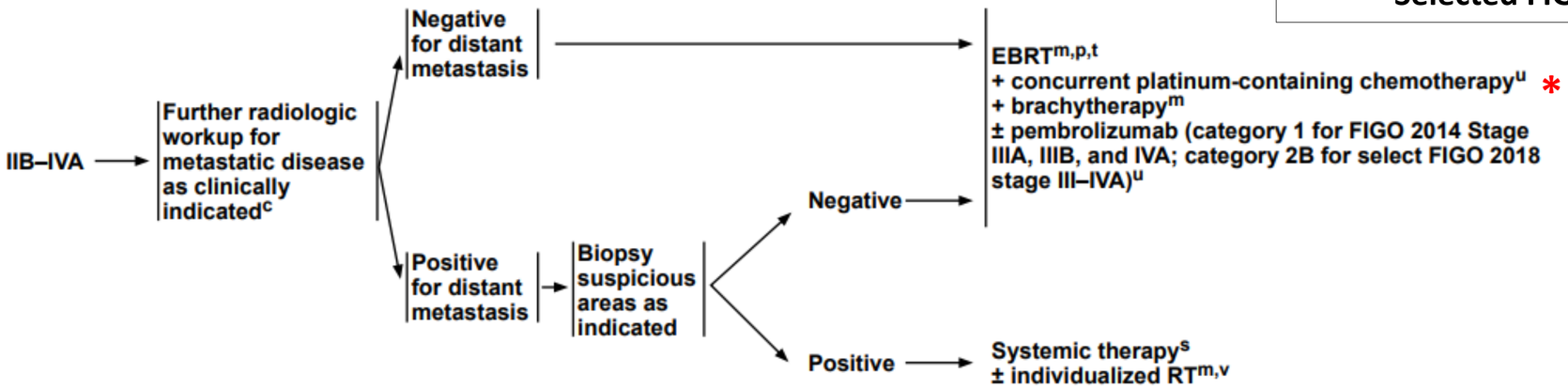
Sustainability?

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2025
Cervical Cancer

NCCN Guidelines Index
Table of Contents
Discussion

CLINICAL STAGE | **PRIMARY TREATMENT**



* **Pembrolizumab may be added:**
  - **FIGO 2014 Stage IIIA-IIIB-IVA (Category 1)**
  - **If FIGO 2018 stage III overlap with FIGO 2014 IIIA/IIIB (Category 1)**
  - **Selected FIGO 2018 Stage IIIC (purely nodal) (Category 2B)**

[c] Principles of Imaging (CERV-B).
[m] Principles of Radiation Therapy (CERV-D).
[p] Induction chemotherapy (carboplatin/paclitaxel) followed by single agent cisplatin (or carboplatin) and radiation given according to the INTERLACE protocol could be considered.(McCormack M, et al. Lancet 2024;404:1525-1535). See Systemic Therapy for Cervical Cancer (CERV-F)
[s] Systemic Therapy for Cervical Cancer (CERV-F).
[t] Extended field RT is recommended when para-aortic nodes are involved by imaging or confirmed on pathology. This may also be added in select patients with positive pelvic nodes such as common iliac metastasis.
[u] Concurrent platinum-containing chemotherapy with EBRT utilizes cisplatin as a single agent (or carboplatin if cisplatin intolerant). Pembrolizumab may be added as follows: Cisplatin (or carboplatin)/RT and pembrolizumab (for FIGO 2014 stage IIIA, IIIB, and IVA: Category 1); Cisplatin (or carboplatin)/RT and pembrolizumab (for select FIGO 2018 stage III–IVA: category 2B). Category 2B is for FIGO 2018 stage IIIC purely on nodal metastasis without concomitant tumor characteristics defined in 2014 FIGO Stage IIIA-IIIB. If the FIGO 2018 staging of stage III overlaps with FIGO 2014 IIIA/IIIB staging, category 1 can be applied to cisplatin (or carboplatin) + pembrolizumab. (See Systemic Therapy for Cervical Cancer [CERV-F]).
[v] Consider ablative therapy for 1–5 metastatic lesions (category 2B) if the primary has been controlled. (Palma DA, et al. Lancet 2019;393:2051-2058.)

Surveillance

THE LANCET

This journal Journals Publish Clinical Global health Multimedia Events About

CORRESPONDENCE · Volume 404, Issue 10467, P2050-2051, November 23, 2024 · Download Full Issue

Pembrolizumab for locally advanced cervical cancer

Maximilian P Schmid [a] · Primoz Petric [b] · Umesh Mahantshetty [c] · Christian Kirisits [a] · Kari Tanderup [d] · Ina Jürgenliemk-Schulz [e] · et al.

THE LANCET

This journal Journals Publish Clinical Global health Multimedia Events About

CORRESPONDENCE · Volume 404, Issue 10467, P2051-2052, November 23, 2024 · Download Full Issue

Pembrolizumab for locally advanced cervical cancer – Authors' reply

Domenica Lorusso [a,b] · Karin Yamada [c] · Kan Li [c] · Annamaria Cerrotta [d] · Gabriella Macchia [e]

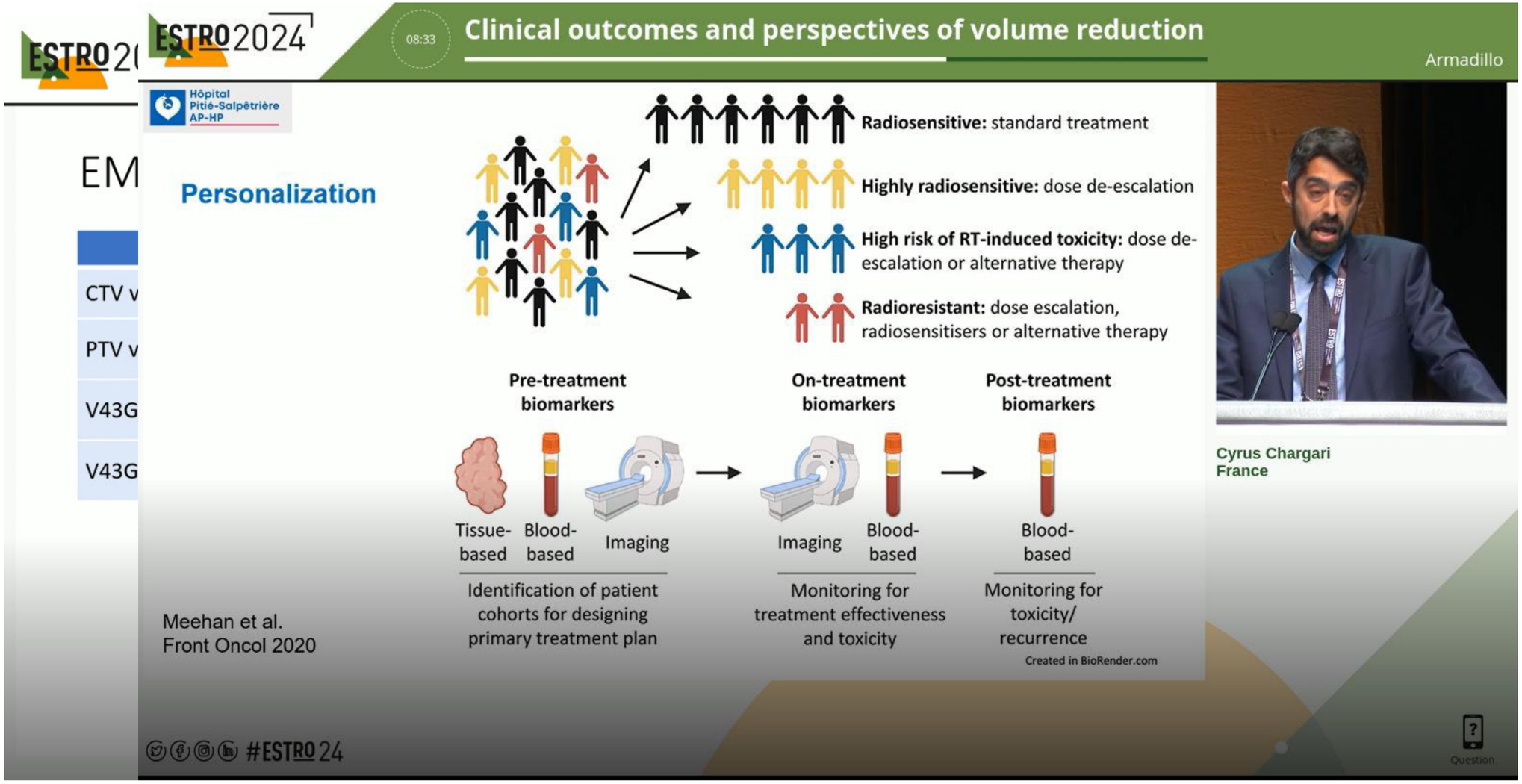
	Keynote A18[1]	EMBRACE –I [2]
	Keynote A18 experimental arm	„KEYMBRACE-I" cohort**
n	529	738
FIGO stage 2014/2009		
IB2-IIB N1	235 (44%)	403 (55%)
III-IV	294 (56%)	335 (45%)
Histology		
Squamous	433 (82%)	634 (86%)
Non-squamous	96 (18%)	103 (14%)
Lymph node status		
Positive pelvic only	326 (62%)	548 (74%)
Positive paraaortic	119 (23%)	98 (13%)
No positive pelvic or paraaortic lymph nodes	84 (16%)	92 (12%)
Median follow-up in months	18	44
24 months PFS / DFS*	68%	71%
24 months OS*	87%	84%

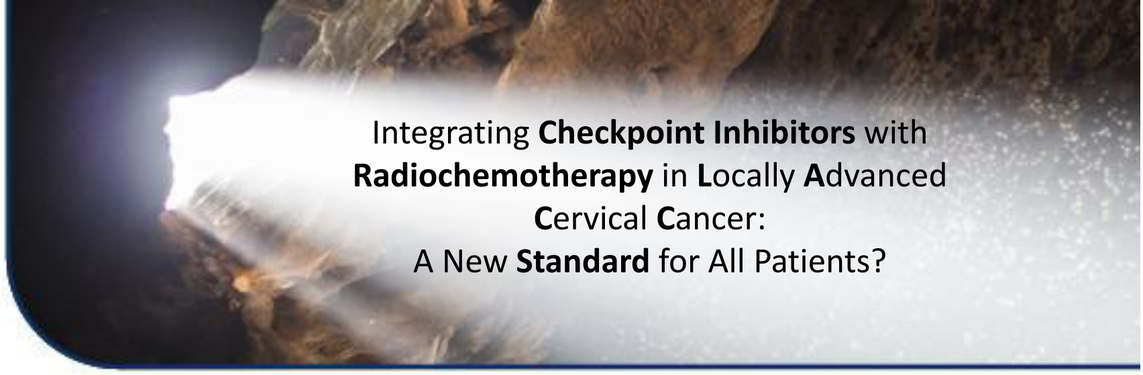
*Progression-free survival (PFS) /disease-free survival (DFS)/ overall survival (OS) at 24 months

What if **brachytherapy** had truly been used to its **full potential** in KEYNOTE-A18? Would the outcomes have told a different story?

Potter R, Tanderup K, Schmid MP, et al. MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicenter prospective cohort study. Lancet Oncol 2021; 22(4): 538-547

Where are we going?





Checkpoint Inhibitors with Radiochemotherapy?

Yes, strong rational and encouraging data

Pembrolizumab in combination with chemoradiotherapy and maintenance is a new standard in LACC?

Yes only for the treatment of FIGO 2014 Stage III - IVA locally advanced cervical cancer in adults who have not received prior definitive therapy. (FDA approved, EMA approved, NCCN guidelines→ waiting for AIFA: to date we have only EAP (expanded access program)

FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

For All Patients?

No, patients have to be selected according to stage, quality of radiotherapy availability, countries resources and reimbursement policy.

Indeed, the true benefit of the combination strategy remains to be investigated

Gemelli
Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

GART
Advanced Radiation Therapy

MRO.ART
MODERN RADIATION ONCOLOGY

MRO.35: Equity and research in oncology. The subtle balance between personalized medicine and accessibility to care

26-27-28 OCTOBER 2025 - Fondazione Policlinico Universitario A. Gemelli IRCCS