Société Marocaine de Cancérologie
الجمعية المغربية لداء السرطان

Post ESTRO 2025
Afrique du Nord
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الجمعية التونسية للأمراض الورمية والعلاج بالأشعة
Société Tunisienne d'Oncologie Radiothérapie

Cancers Gynécologiques et mammaires

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University of Keele, UK

FAST-Forward

ESTRO 2025

Hypofractionated breast radiotherapy for 1 week vs 3 weeks: 10-year efficacy and late normal tissue effects in the FAST-Forward randomised trial

AM Brunt, FH Cafferty, J Patel, MA Sydenham, A Alhasso, DJ Bloomfield, C Chan, M Churn, S Cleator, CE Coles, H Fleming, A Goodman, C Griffin, JS Haviland, AM Kirby, C Kirwan, Z Nabi, K Poole, E Sawyer, N Somaiah, I Syndikus, D Wheatley, JR Yarnold, JM Bliss on behalf of the FAST-Forward Trial Management Group

FUNDED BY NIHR | National Institute for Health and Care Research

ICR The Institute of Cancer Research

Primary analysis: 5-year outcomes (reported 2020[1])

- **Non-inferior IBR** in both 5-fraction groups (against pre-specified NI margin, 1.6%)

	No. events	5yr estimate (95% CI)	Difference vs. 40 Gy (95%CI)
40 Gy	31	2.1% (1.4, 3.1)	-
27 Gy	27	1.7% (1.2, 2.6)	-0.3% (-1.0, 0.9)
26 Gy	21	1.4% (0.9, 2.2)	-0.7% (-1.3, 0.3)

- For **late effects**
  - 26Gy/5Fr similar to 40Gy/15Fr
  - 27Gy/5Fr consistent with 50Gy/25Fr

1. AM Brunt, et al. The Lancet 2020, Volume 395, Issue 10237, 1613 - 1626

Current analysis: 10-years

- Median follow-up 10.0 years (IQR:10.0-10.2)
- Efficacy and normal tissue effects by 10 years
- Estimation of effects - no pre-specified hypothesis testing

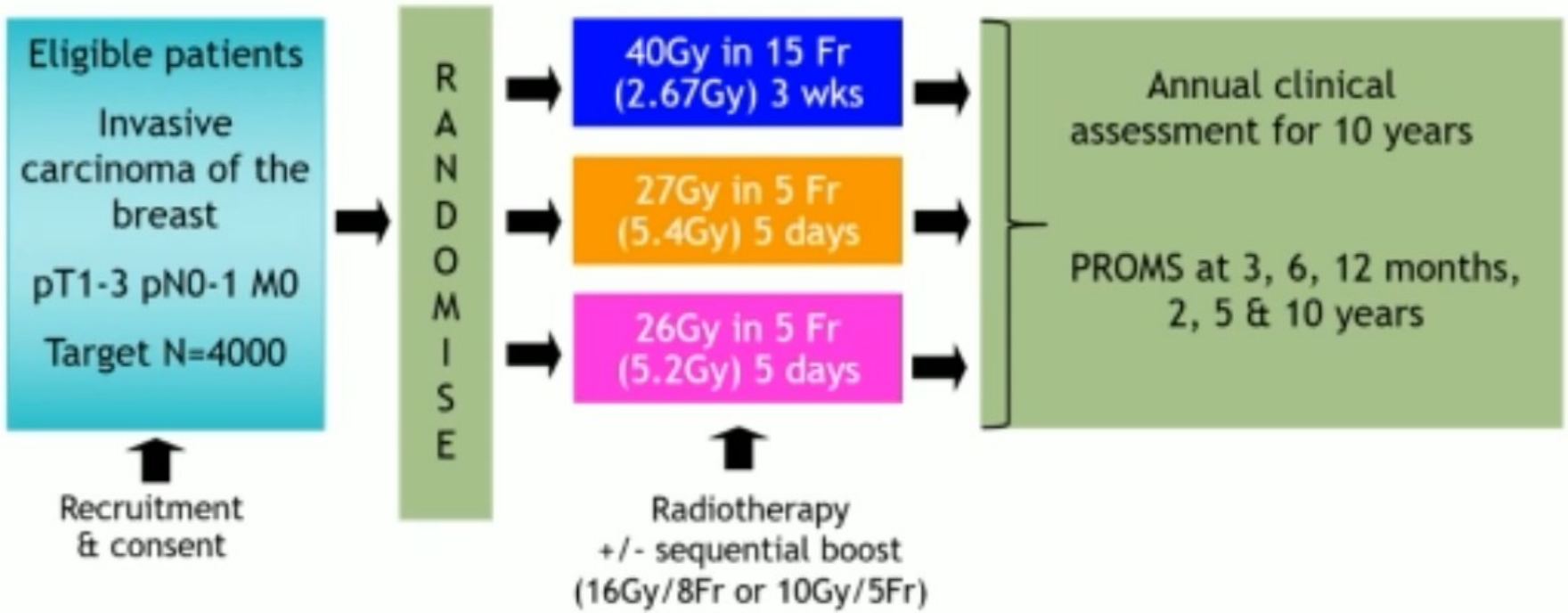
FAST-Forward trial: Aim

To test a 1-week course of curative whole breast radiotherapy

against a standard 3-week schedule in terms of local cancer control

and late adverse effects in patients with early breast cancer

FAST-Forward trial design



Primary endpoint: Ipsilateral breast recurrence (IBR); primary analysis tested non-inferiority at 5 years

Secondary endpoints: Patient- and clinician-reported normal tissue effects, other breast cancer events, survival, quality of life

Patients: Baseline and treatment details

N = 4096 recruited from 97 UK centres, Nov 2011 - Jun 2014

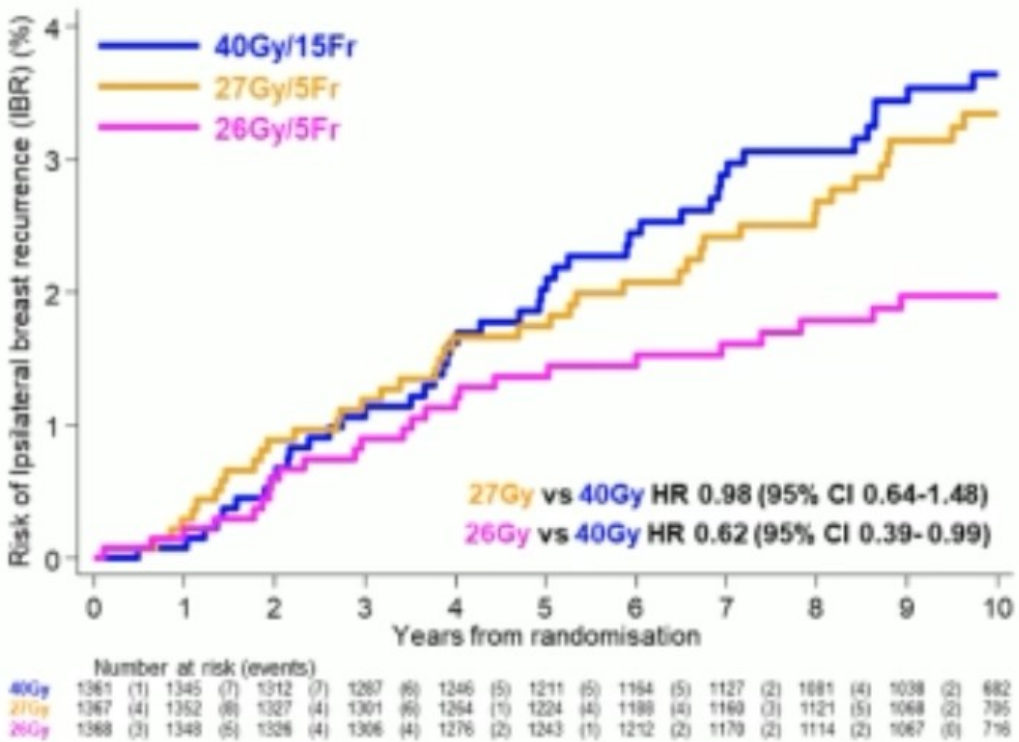
		40Gy in 15Fr N=1361 (%)	27Gy in 5Fr N=1367 (%)	26Gy in 5Fr N=1368 (%)
Age (years)	Median (range)	60 (29-89)	61(25-90)	61(25-89)
Grade	1	23	23	22
	2	49	49	50
	3	28	28	28
Risk group	Low (age≥50 & G1 or 2)	62	63	62
	High (age<50 or G3)	38	37	38
Primary surgery	Breast conservation	93	94	94
	Mastectomy	7	6	6
Pathological node status	Positive	19	18	19
	Negative	81	82	81
ER / HER2 status	ER+ / HER2+	8	8	7
	ER+ / HER2-	82	83	81
	ER- / HER2+	3	2	3
	ER- / HER2-	7	7	9
Tumour bed boost	No	75	75	76
	Yes	25	25	24
Boost dose	10Gy in 5Fr	76	81	77
	16Gy in 8Fr	24	19	23

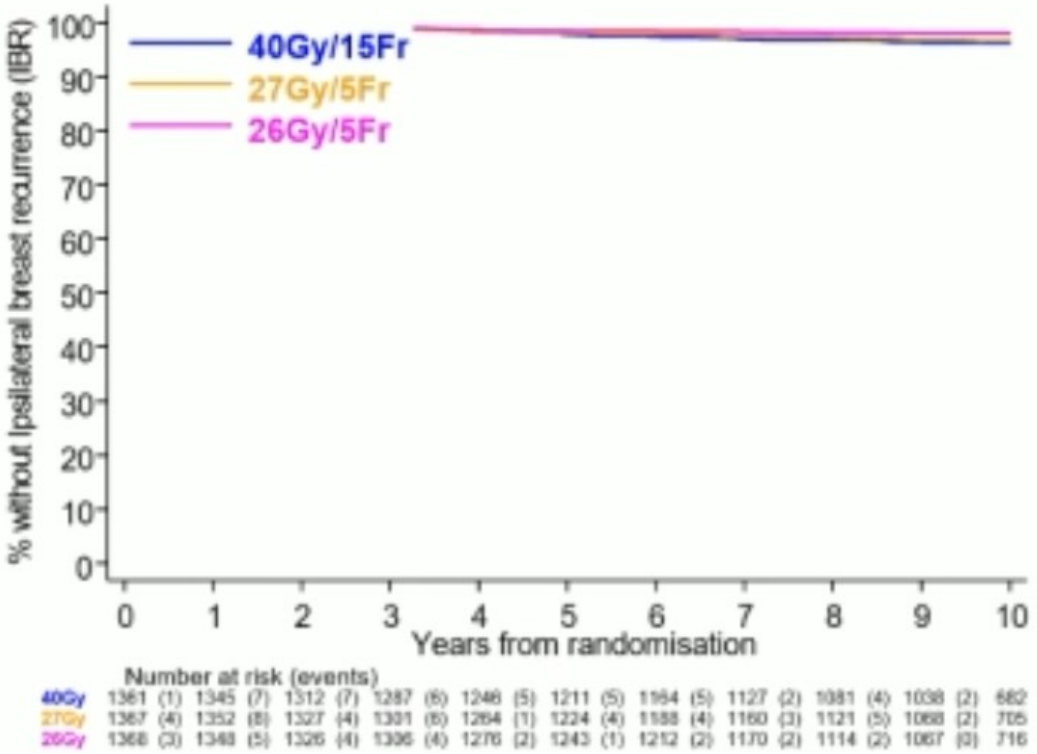
Ipsilateral breast recurrence (primary endpoint)

	40Gy in 15Fr N=1361	27Gy in 5Fr N=1367	26Gy in 5Fr N=1368
Number of IBR events	44	44	28
10-year cumulative IBR estimate, % (95% CI)	3.6 (2.7, 4.8)	3.3 (2.4, 4.4)	2.0 (1.3, 2.9)
Hazard ratio (95% CI)	-	0.98 (0.64, 1.48)	0.62 (0.39, 0.99)
Difference (smoothed estimate) in 10-yr IBR vs control, % (95% CI)	-	-0.08 (-1.3, 1.7)	-1.3 (-2.2, -0.02)

Events: Recurrence (non-invasive or invasive) or new primary in the ipsilateral breast

Ipsilateral breast recurrence (primary endpoint)





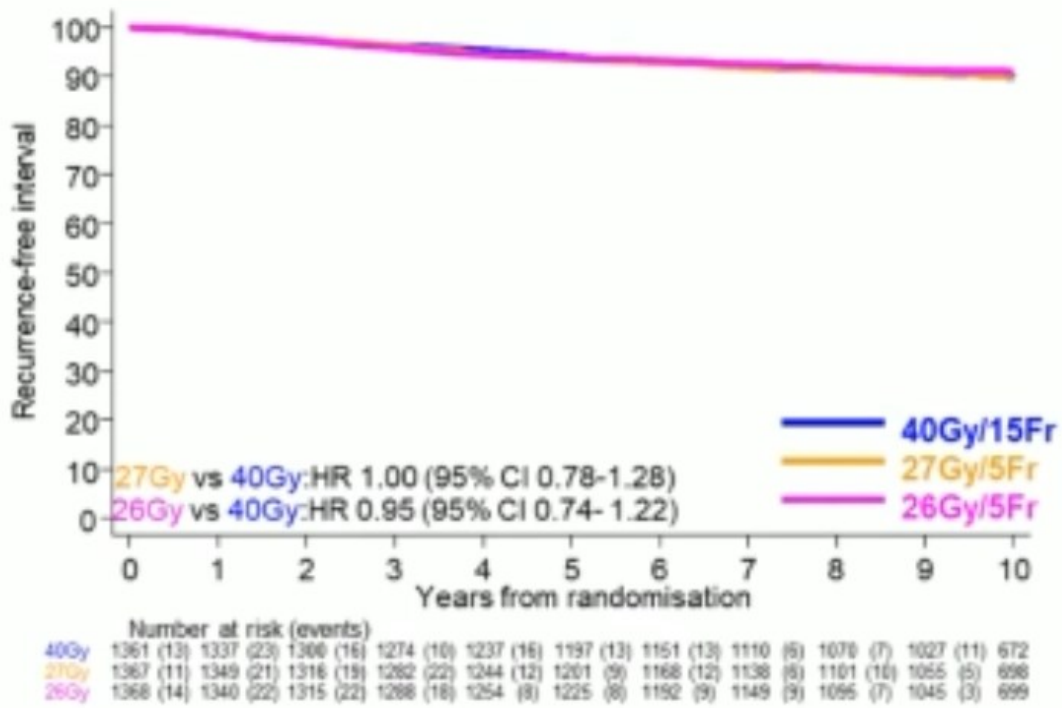
Events: Recurrence (non-invasive or invasive) or new primary in the ipsilateral breast

Summary of disease events by 10 years

	40Gy in 15Fr N=1361	27Gy in 5Fr N=1367	26Gy in 5Fr N=1368
Ipsilateral breast recurrence (IBR)	44	44	28
Locoregional recurrence	57	56	45
Distant recurrence	87	88	102
New contralateral primary	35	36	31
Other second primary	73	77	83
Deaths - all causes	195	214	202
Breast cancer death	77	79	74
Other cause death*	118	135	128

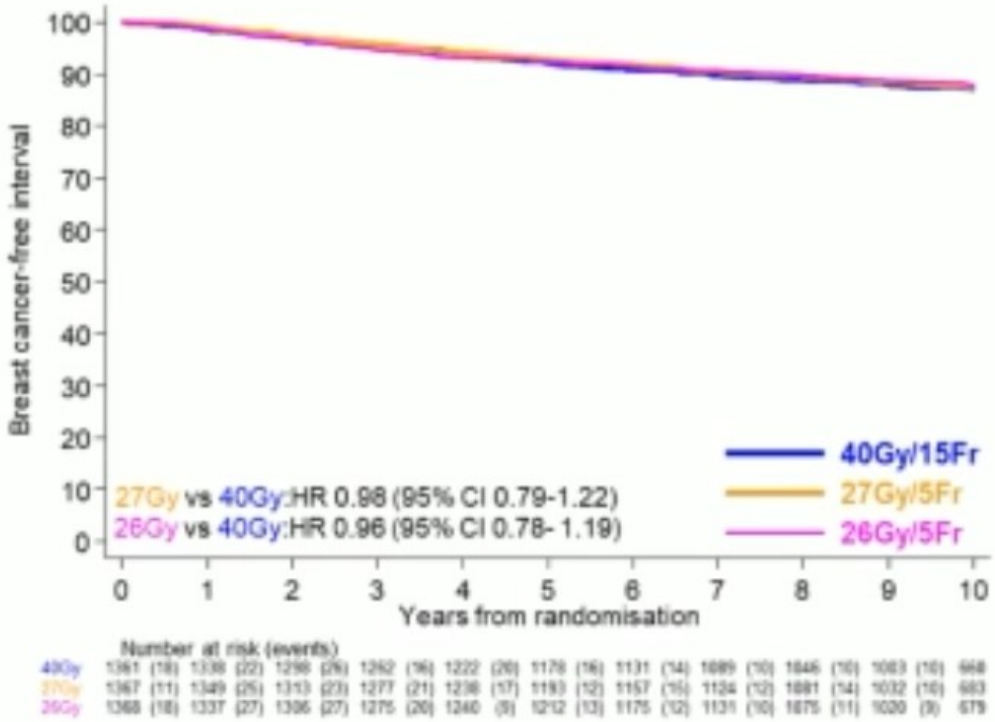
*Includes unknown cause of deaths (17 in 40Gy, 17 in 27Gy, 16 in 26Gy)

Recurrence-free interval



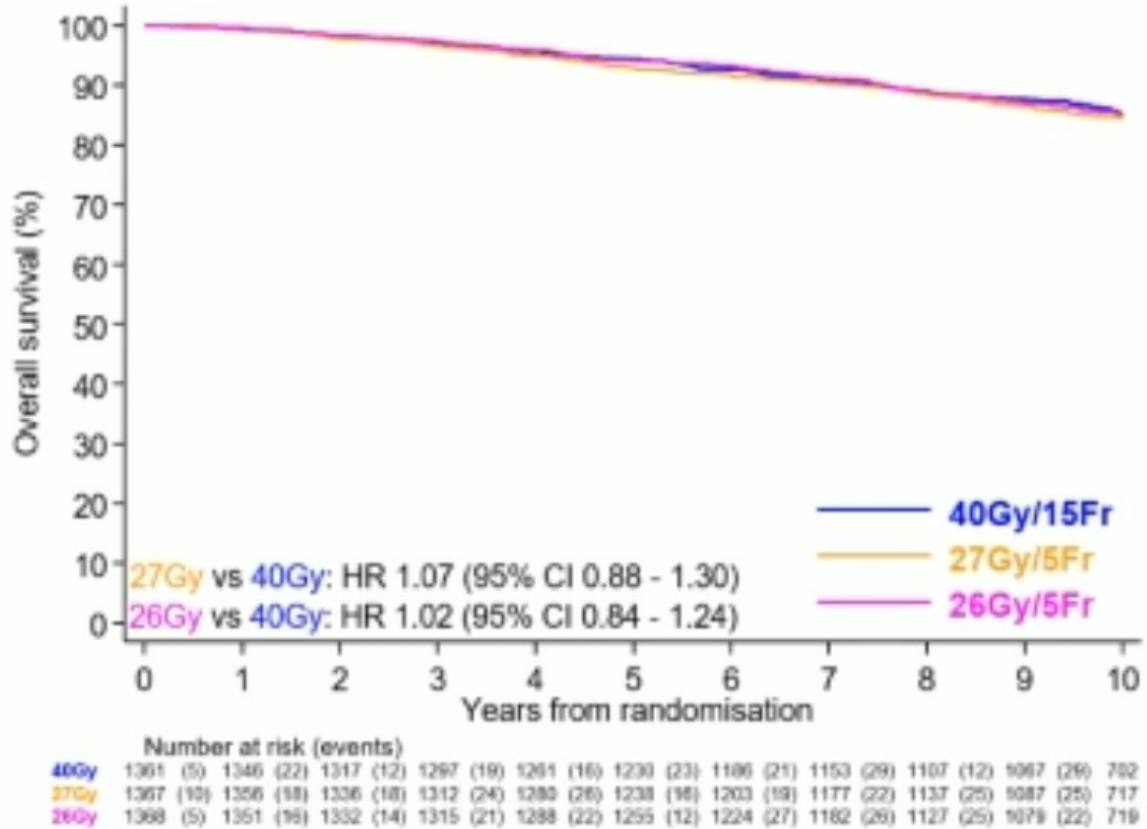
Events: IBR or regional recurrence (non-invasive or invasive), distant recurrence, death from breast cancer

Breast cancer-free interval



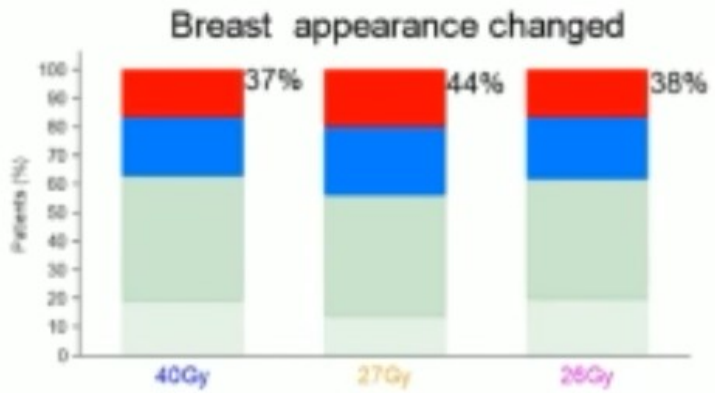
Events: DCIS or invasive IBR, locoregional invasive recurrence, distant recurrence, DCIS or invasive contralateral cancer, death from breast cancer

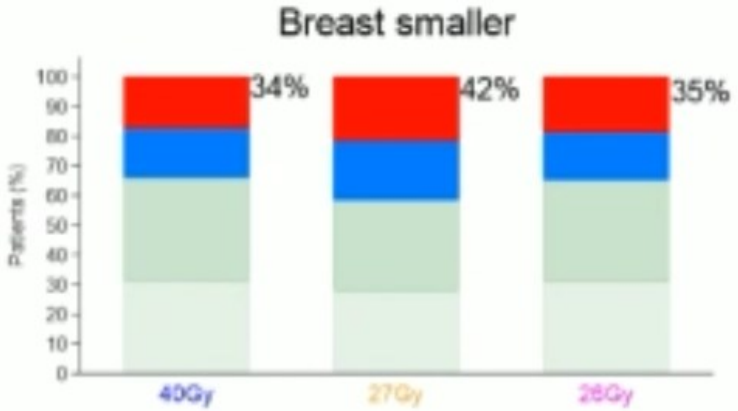
Overall survival



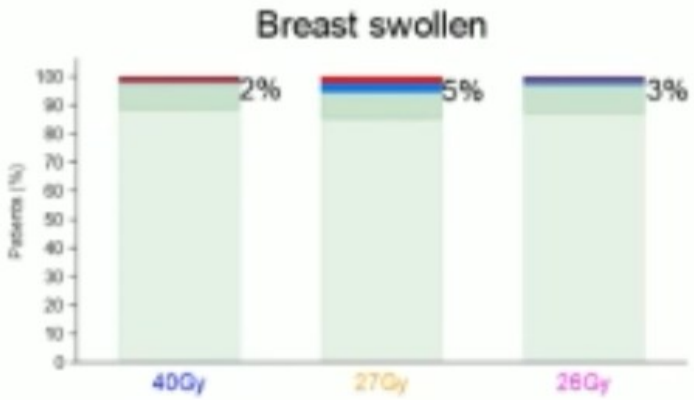
Events: Death from any cause

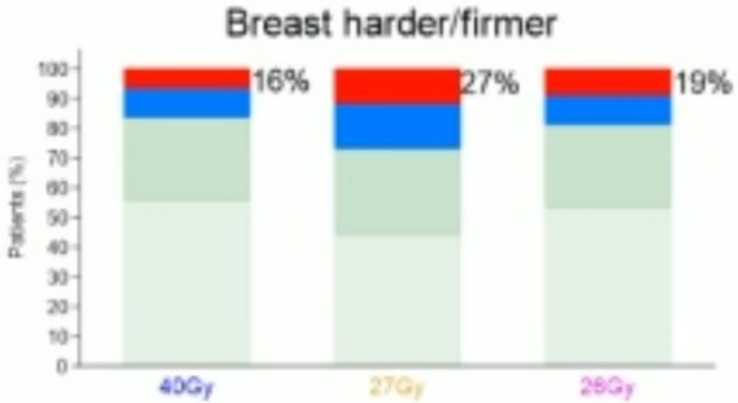
Patient-reported breast symptoms at 10 years (N = 1,742)



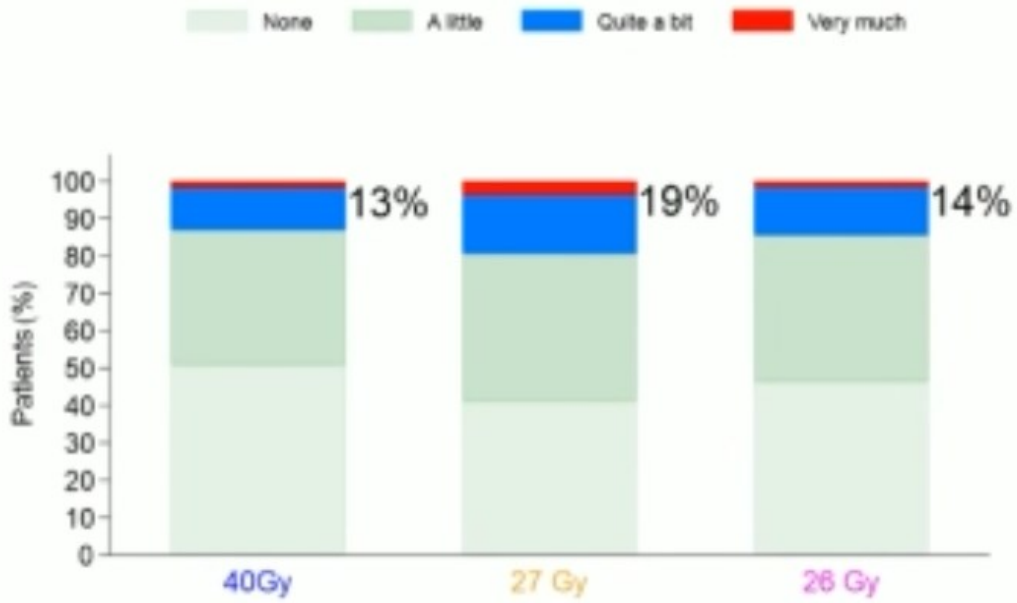


The % of patients with moderate or marked symptoms ("quite a bit" or "very much") is indicated



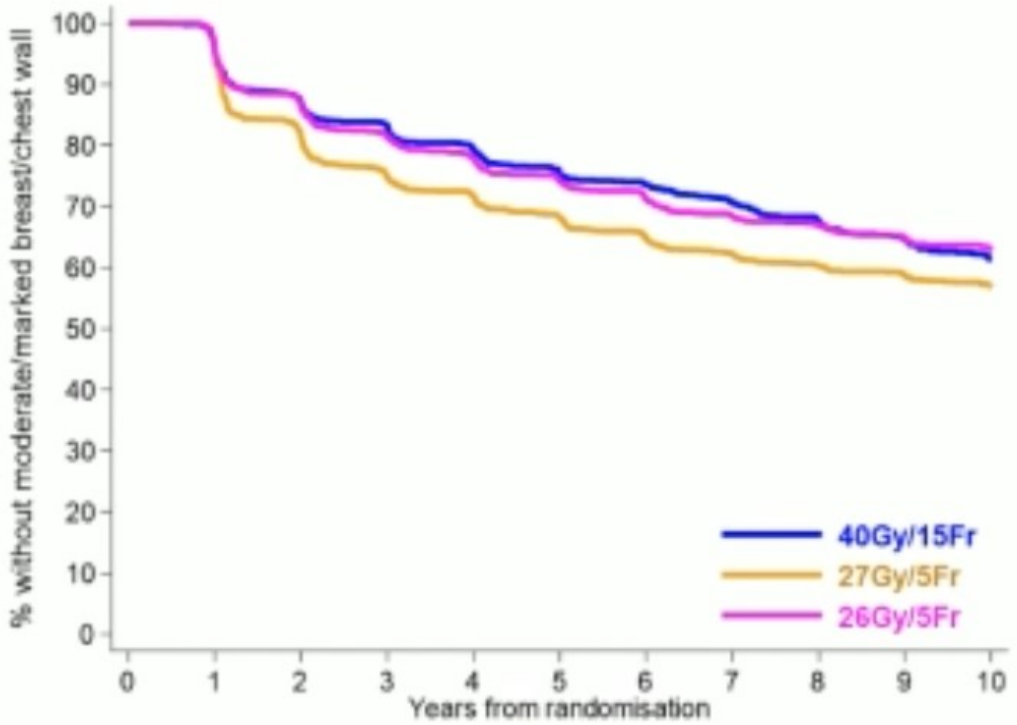


Breast/chest wall symptoms* at 10-years
(Clinician-reported, N = 2,345)



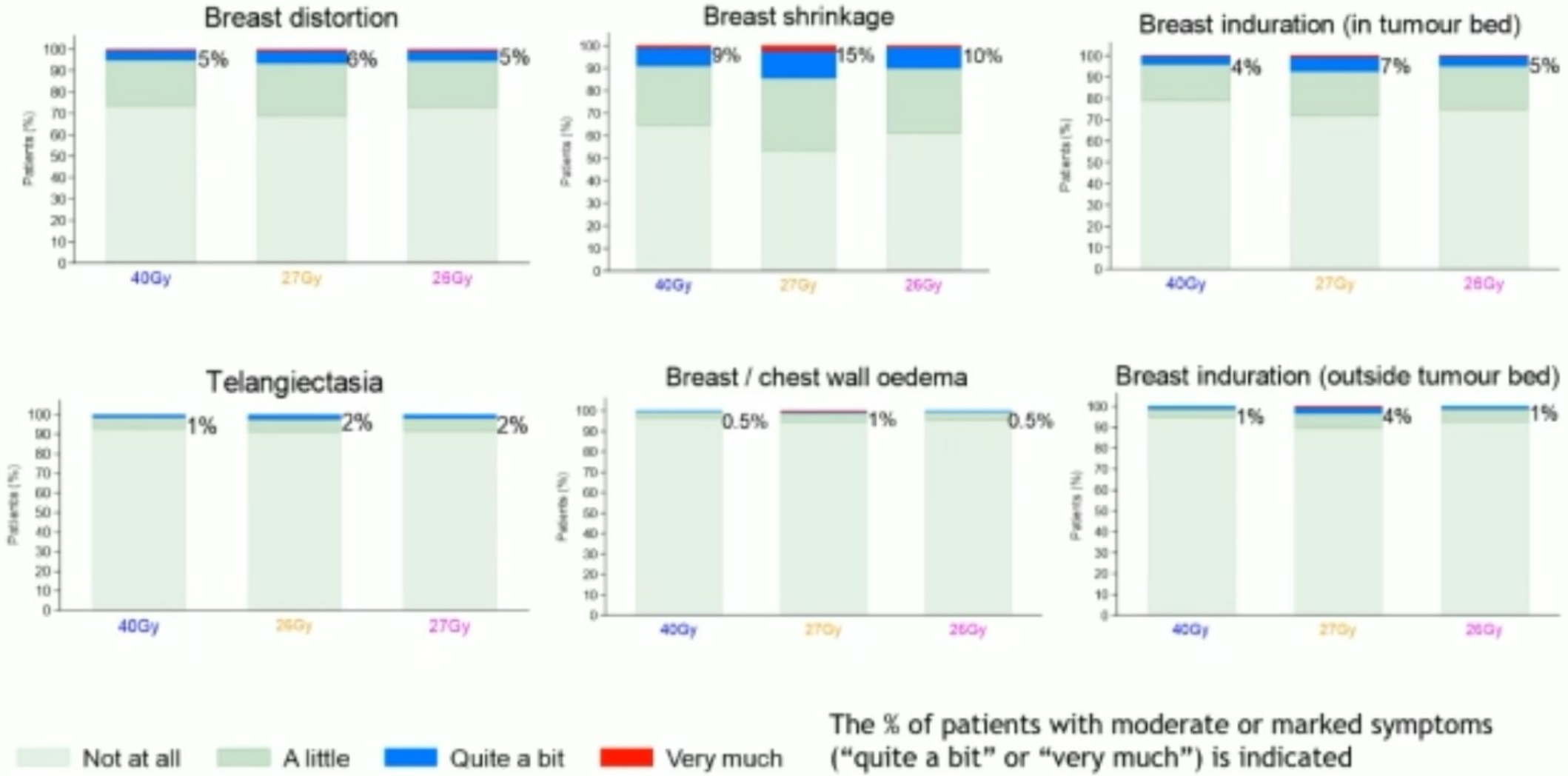
%s are those with moderate or marked effects

Time to moderate or marked breast/chest wall symptoms*
(Clinician-reported, N=3,987)



* Includes breast distortion, breast shrinkage, breast induration (inside or outside tumour bed), telangiectasia and breast/chest wall oedema; Moderate = “Quite a bit”; Marked = “Very much”

Clinician-reported breast symptoms at 10 years (n=2,345)



Incidence of other late adverse effects

Confirmed cases	40Gy in 15Fr N=1361 (%)	27Gy in 5Fr N=1367 (%)	26Gy in 5Fr N=1368 (%)
Symptomatic rib fracture	10 (0.7)	19 (1.4)	15 (1.1)
Ipsilateral side	*8 (0.6)*	*17 (1.2)*	*10 (0.7)*
Symptomatic lung fibrosis	11 (0.8)	13 (1.0)	10 (0.7)
Ipsilateral side	*4 (0.3)*	*8 (0.6)*	*7 (0.5)*
Ischaemic heart disease	21 (1.5)	17 (1.2)	20 (1.5)
Left-sided	*8 (0.6)*	*11 (0.8)*	*8 (0.6)*

Conclusions

- Low incidence of IBR across all schedules
- Patient and clinician-reported late effects similar for 26Gy/5Fr and 40Gy/15Fr
- Results confirm 26Gy/5Fr as appropriate SOC
    - Breast
    - Chest wall
    - Partial breast
- Ongoing analyses will further explore normal tissue effects reported over time

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FAST-Forward

ESTRO 2025

FAST-Forward nodal sub-study: 5-year normal tissue effects following 1-week versus 3-week axillary radiotherapy for breast cancer

AM Brunt, D Wheatley, J Patel, FH Cafferty, MA Sydenham, A Alhasso, C Chan, S Cleator, CE Coles, H Fleming, D Gahir, A Goodman, JS Haviland, AM Kirby, C Kirwan, Z Nabi, E Sawyer, J Sinclair, N Somaiah, I Syndikus, K Venables, JR Yarnold, JM Bliss on behalf of the FAST-Forward Trial Management Group

FUNDED BY
NIHR | National Institute for Health and Care Research

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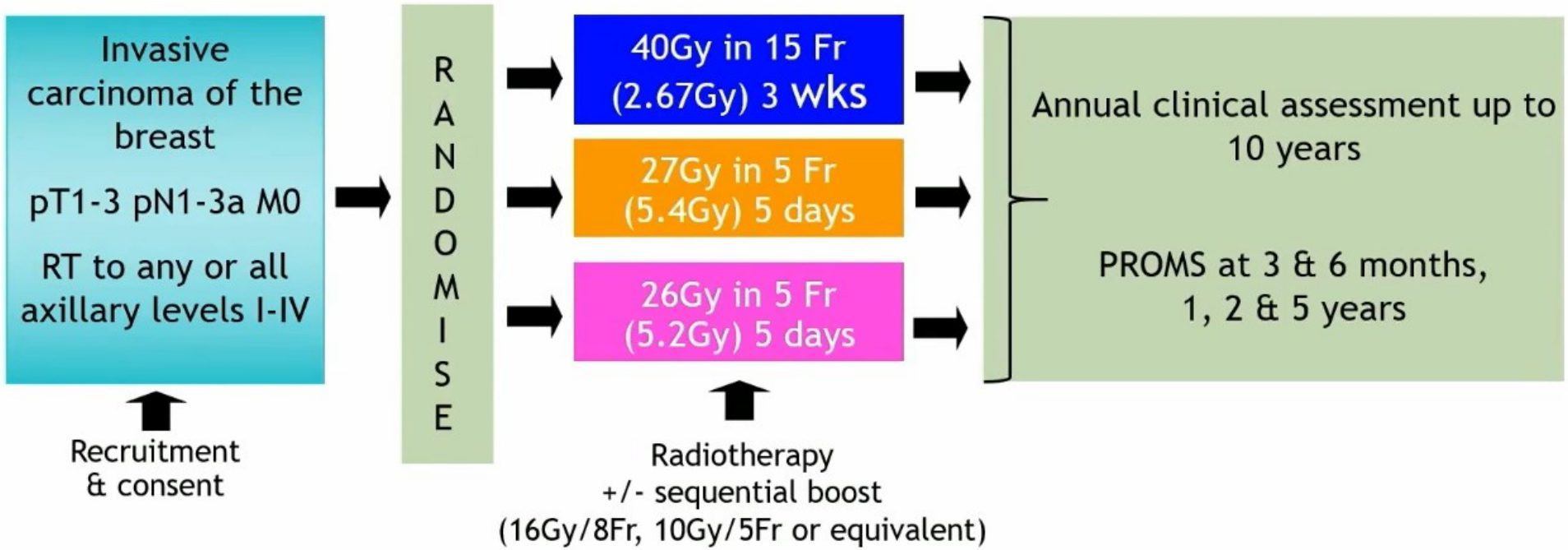
FAST-Forward nodal sub-study: Aim

To test the safety of a 1-week schedule of adjuvant radiotherapy to level I-IV axilla compared with a standard 3-week schedule in terms of late normal tissue effects (NTEs) at 5 years in patients with early breast cancer requiring nodal radiotherapy

FAST-Forward nodal sub-study: Design



Primary endpoint: Patient-reported arm/hand swelling (EORTC-QLQ-BR23) at 5 years

Secondary endpoints: Patient- and clinician-reported normal tissue effects, with a focus on arm/shoulder symptoms; quality of life; breast cancer events and survival

Hypothesis and current analysis

- Main trial: 26Gy/5Fr similar to 40Gy/15Fr; 27Gy/5Fr consistent with 50Gy/25Fr
- 27Gy/5Fr sub-study group closed early after analysis of 3-year NTEs in main trial
- Current analysis focuses on 26Gy/5Fr vs 40Gy/15Fr; 5-year NTEs
- 10% moderate or marked arm/hand swelling expected with 40Gy/15Fr; aim to exclude 20% (+10%) with 26Gy/5Fr (90% power, one-sided α=0.05)
- Target n= 172 in each of 40Gy/15Fr and 26Gy/5Fr
- 469 recruited (181 40Gy/15Fr, 182 26Gy/5Fr, 104 27Gy/5Fr); median follow-up 76 mths

Patients: Baseline and treatment details

		40Gy/15Fr N=181 (%)	26Gy/5Fr N=182 (%)
Age (years)	Median (IQR)	61 (52-72)	60 (51-70)
Grade	1	15 (8)	12 (7)
	2	95 (52)	97 (53)
	3	71 (39)	73 (40)
Primary surgery	Breast conservation	95 (52)	106 (58)
	Mastectomy	86 (48)	76 (42)
ER / HER2 status	ER+ / HER2+	29 (16)	27 (15)
	ER+ / HER2-	124 (68)	122 (67)
	ER- / HER2+	7 (4)	6 (3)
	ER- / HER2-	21 (12)	24 (13)
Side of primary	Left	87 (48)	104 (57)
	Right	94 (52)	78 (43)
Tumour bed boost	% of those with breast conservation surgery	46 (48)	47 (44)

Patients: Baseline and treatment details

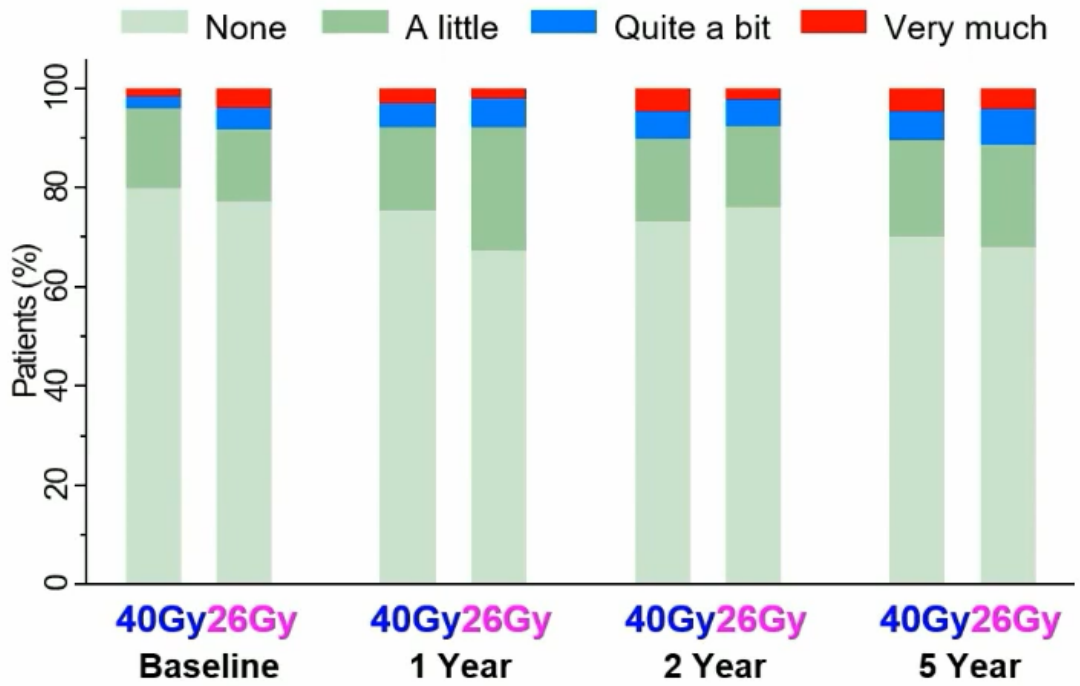
		40Gy/15Fr N=181 (%)		26Gy/5Fr N=182 (%)	
Axillary lymph node dissection (ALND)	Yes	106	(59)	91	(50)
	No	75	(41)	91	(50)
Nodal areas irradiated	Axilla level I	82	(46)	91	(51)
	Axilla level II	91	(51)	95	(53)
	Axilla level III	123	(69)	126	(70)
	Axilla level IV (SCF)	161	(91)	164	(91)
	IMC	0	(0)	1	(<1)
	Missing on form	1		2	

Patient-reported arm/hand swelling (primary endpoint)

(n= 107 40Gy/15, n=116 26Gy/5 with 5-year data)

Moderate or marked arm/hand swelling

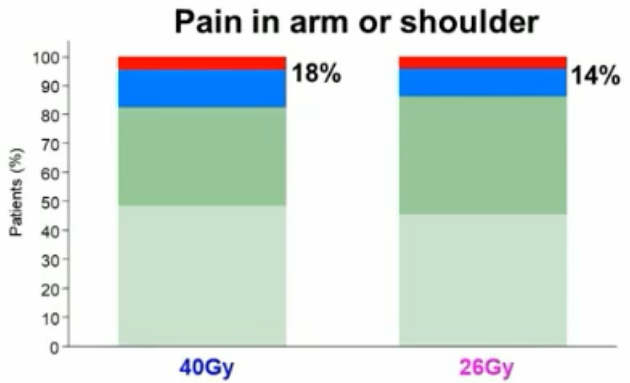
ITT	40Gy/15Fr	26Gy/5Fr
Events at 5 years (%)	11 (10)	13 (11)
% difference vs 40Gy/15 (90% CI), p-value	-	1 (-6, 8) p=0.49
Per protocol		
Events at 5 years (%)	11 (11)	13 (11)
% difference vs 40Gy/15 (90% CI), p-value	-	1 (-7, 8) p=0.41

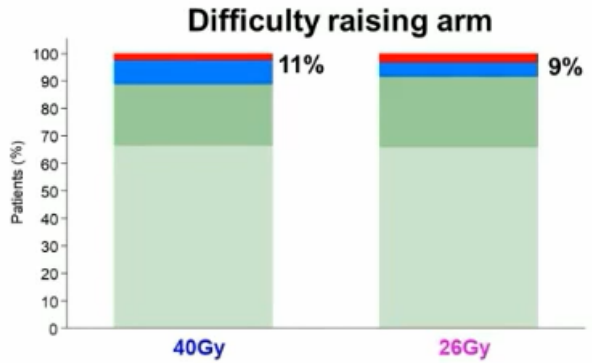


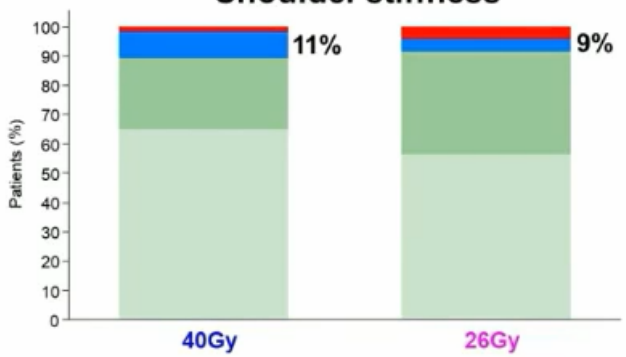
Number of patients

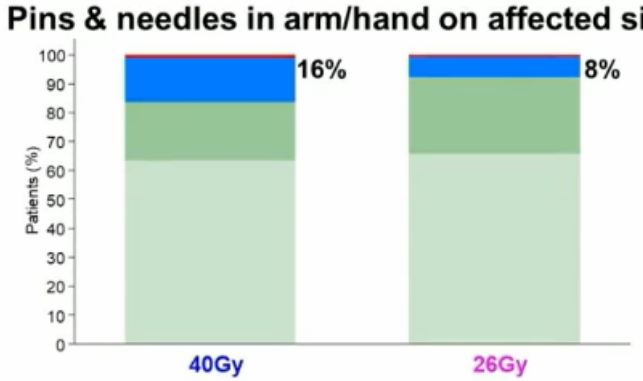
40Gy	180	130	127	107
26Gy	181	141	134	116

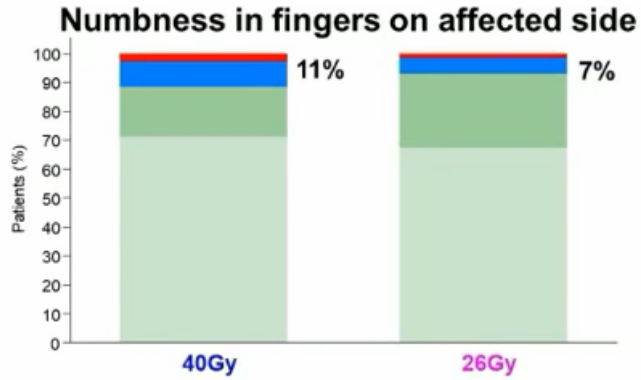
Patient-reported arm/shoulder symptoms at 5 years

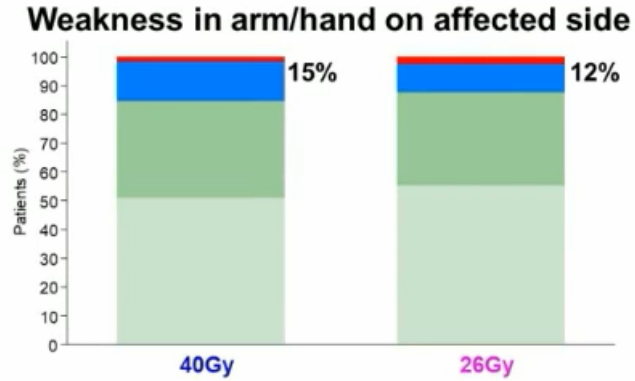








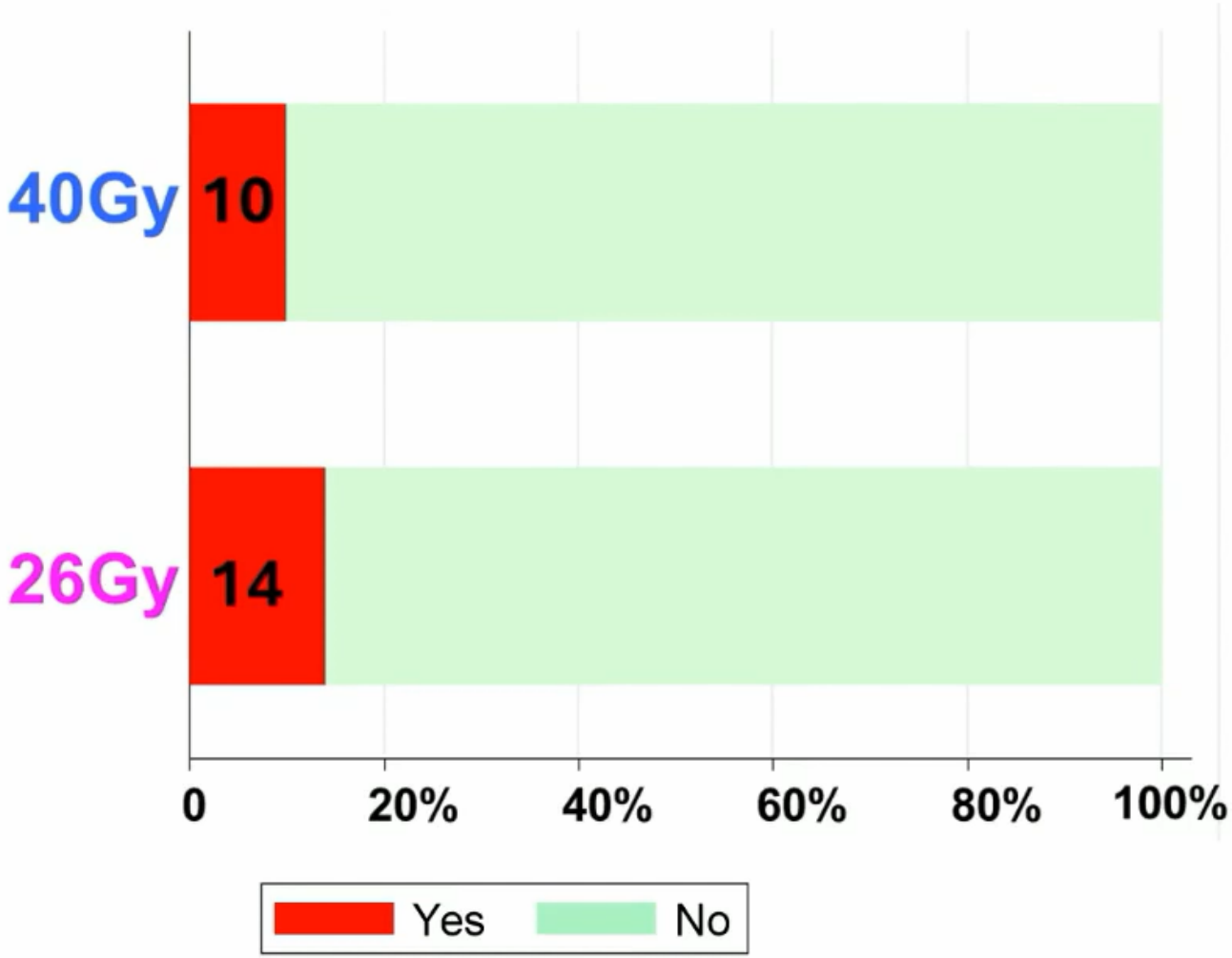




Not at all A little Quite a bit Very much

The % of patients with moderate or marked symptoms ("quite a bit" or "very much") is shown

Clinician-assessed arm lymphoedema at 5 years (N=289)



No cases of brachial plexopathy in any treatment group (including 27 Gy)

Conclusions

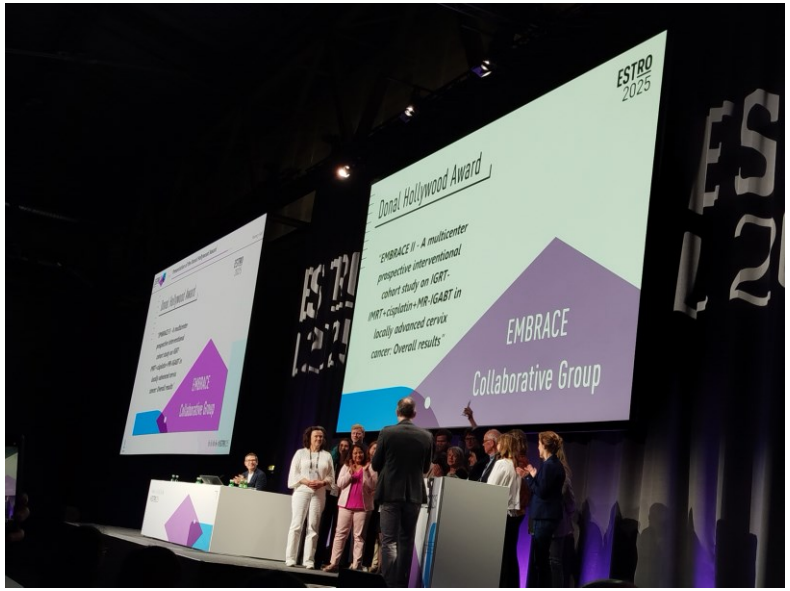
- 26Gy/5 non-inferior to 40Gy/15 terms of patient-reported arm/hand swelling
- Other NTEs reported by patients and clinicians were similar for the two schedules
- No cases of radiation-induced brachial plexopathy
- 26Gy in 5 daily fractions is safe for patients requiring adjuvant radiotherapy to the axilla (along with breast/chest wall)
- Efficacy endpoints will be analysed in conjunction with the main trial (n=4096); low recurrence rates expected based on 5- and 10-year results in main trial

EMBRACE-I: Long-Term Results

Primoz Petric, Alina Sturdza, Stefan Ecker, Maximilian Schmid, Christian Kirisits, Jacob Lindegaard, Ina Schulz-Jurgenliemk, Kari Tanderup, Barbara Šegedin, Kjersti Bruheim, Fleur Huang, Bhavana Rai, Elzbieta van der Steen-Banasik, Maarit Anttila, Marit Sundset, Richard Pötter

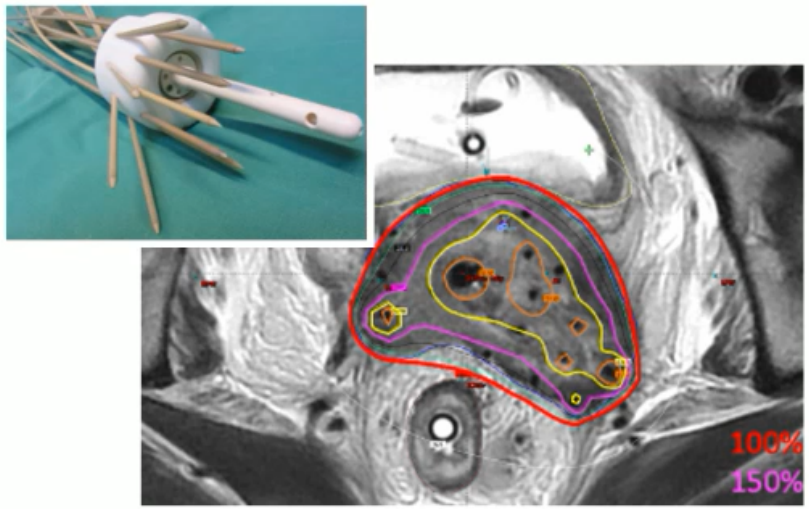
Primoz Petric, Switzerland

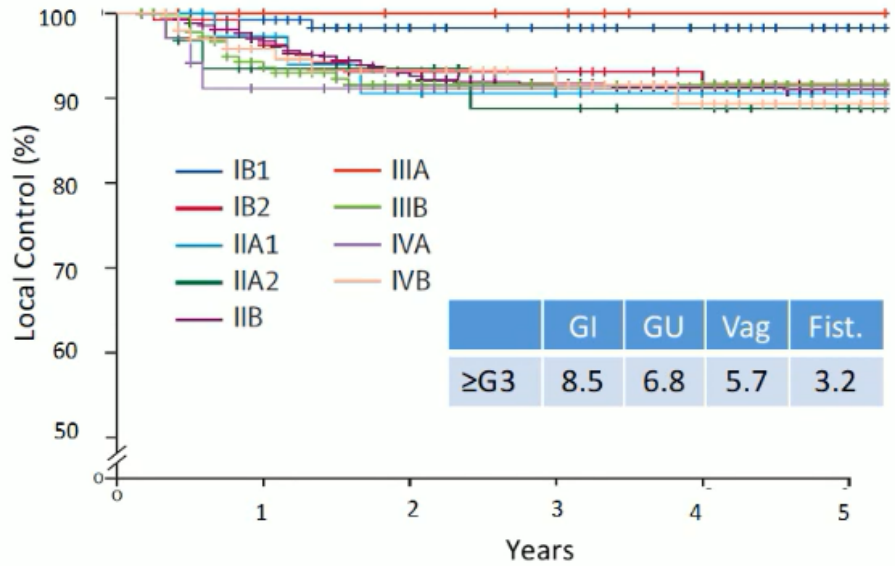
luzerner kantonsspital



Background: EMBRACE I Results of IGABT

Pötter R, et al. Lancet Oncol, 2021





	Median FU (months)	Actuarial Rate	Local Control	Pelvic Control	Disease-free Survival	Overall Survival
EMBRACE-I; *2021 (N=1341)*	51	@ 5 years	92%	87%	86%	74%

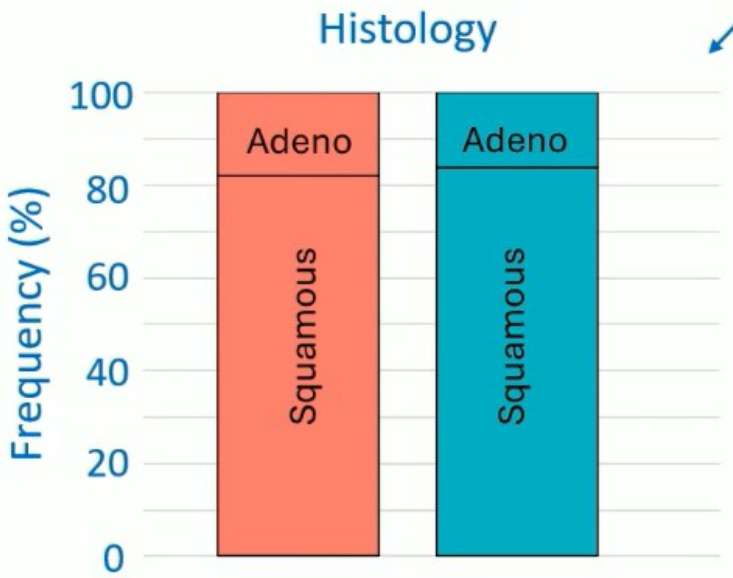
luzerner kantonsspital

Results

EMBRACE-I Original Cohort *2021 (N=1341)*

Vs.

EMBRACE-I Extended FU Cohort *2024 (N=609)*



Characteristic	Overall N = 1,341[1]	Long-term cohort N = 610[1]	Other N = 731[1]
histopathological_type_sta_d			
SQ	1,097 (82%)	511 (84%)	586 (80%)
AC	192 (14%)	80 (13%)	112 (15%)
AdSq	50 (3.7%)	19 (3.1%)	31 (4.3%)
FIGO			
2A	69 (5.1%)	18 (3.0%)	51 (7.0%)
3A	13 (1.0%)	6 (1.0%)	7 (1.0%)
4A	34 (2.5%)	9 (1.5%)	25 (3.4%)
2B	693 (52%)	369 (60%)	324 (44%)
3B	190 (14%)	84 (14%)	106 (15%)
4B	98 (7.3%)	44 (7.2%)	54 (7.4%)
1B1	124 (9.3%)	38 (6.2%)	86 (12%)
1B2	119 (8.9%)	42 (6.9%)	77 (11%)
age	49 (41, 60)	50 (41, 61)	49 (41, 60)
who_score_sta_d			
PS0	969 (72%)	473 (78%)	496 (68%)
PS1	339 (25%)	125 (20%)	214 (29%)
PS2	29 (2.2%)	11 (1.8%)	18 (2.5%)
PS3	3 (0.2%)	1 (0.2%)	2 (0.3%)
PS4	0 (0%)	0 (0%)	0 (0%)
pathological_nodes_present	699 (52%)	320 (52%)	379 (52%)
ebrtptv_e_volume_tdvh	1,615 (1,357, 1,899)	1,733 (1,512, 2,012)	1,474 (1,250, 1,767)
ebrtptv_e_technique_tdvh			
1	788 (59%)	356 (59%)	432 (59%)
2	550 (41%)	252 (41%)	298 (41%)
ebrtptv_e_total_dose_prescribed_tdvh	45.00 (45.00, 46.00)	45.00 (45.00, 46.10)	45.00 (45.00, 46.00)
conc_chemo_given_tdvh	1,265 (95%)	566 (93%)	699 (96%)
bt_dose_rate			
HDR	765 (57%)	318 (52%)	447 (61%)
PDR	571 (43%)	289 (48%)	282 (39%)
ctv-hr-volume	29 (21, 41)	30 (22, 42)	28 (19, 41)
total_hrctv_d90	90 (85, 94)	91 (87, 95)	88 (83, 93)
total_gtv_d98	99 (89, 111)	102 (94, 113)	96 (87, 110)
total_irctv_d98	63.3 (61.1, 65.9)	64.4 (62.0, 66.8)	62.6 (60.3, 65.3)
total_bladder_d2cc	76 (69, 83)	74 (69, 82)	78 (70, 84)
total_icru_bladder	65 (57, 76)	65 (56, 74)	66 (57, 78)
total_rectum_d2cc	62 (57, 68)	62 (57, 66)	63 (58, 69)
total_icru_rectum	65 (60, 71)	64 (60, 68)	66 (60, 73)
total_sigmoid_d2cc	64 (59, 69)	65 (61, 69)	63 (58, 68)
total_bowel_d2cc	63 (56, 69)	63 (57, 69)	63 (56, 71)

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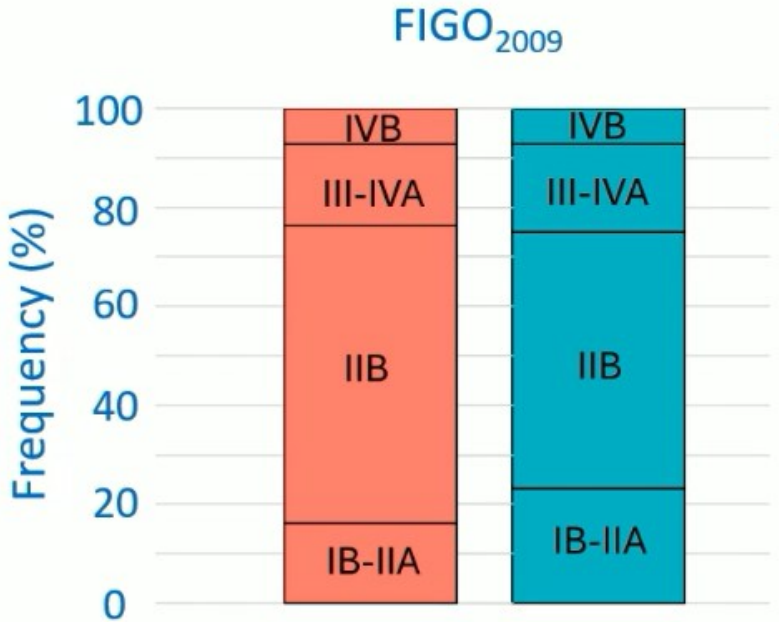
Results

EMBRACE-I Original Cohort *2021 (N=1341)*

Vs.

EMBRACE-I Extended FU Cohort *2024 (N=609)*



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histopathological_type_sta_d			
SQ	1,097 (82%)	511 (84%)	586 (80%)
AC	192 (14%)	80 (13%)	112 (15%)
AdSq	50 (3.7%)	19 (3.1%)	31 (4.3%)
FIGO			
2A	69 (5.1%)	18 (3.0%)	51 (7.0%)
3A	13 (1.0%)	6 (1.0%)	7 (1.0%)
4A	34 (2.5%)	9 (1.5%)	25 (3.4%)
2B	693 (52%)	369 (60%)	324 (44%)
3B	190 (14%)	84 (14%)	106 (15%)
4B	98 (7.3%)	44 (7.2%)	54 (7.4%)
1B1	124 (9.3%)	38 (6.2%)	86 (12%)
1B2	119 (8.9%)	42 (6.9%)	77 (11%)
age	49 (41, 60)	50 (41, 61)	49 (41, 60)
who_score_sta_d			
PS0	969 (72%)	473 (78%)	496 (68%)
PS1	339 (25%)	125 (20%)	214 (29%)
PS2	29 (2.2%)	11 (1.8%)	18 (2.5%)
PS3	3 (0.2%)	1 (0.2%)	2 (0.3%)
PS4	0 (0%)	0 (0%)	0 (0%)
pathological_nodes_present	699 (52%)	320 (52%)	379 (52%)
ebrtptv_e_volume_tdvh	1,615 (1,357, 1,899)	1,733 (1,512, 2,012)	1,474 (1,250, 1,767)
ebrtptv_e_technique_tdvh			
1	788 (59%)	356 (59%)	432 (59%)
2	550 (41%)	252 (41%)	298 (41%)
ebrtptv_e_total_dose_prescribed_tdvh	45.00 (45.00, 46.00)	45.00 (45.00, 46.10)	45.00 (45.00, 46.00)
conc_chemo_given_tdvh	1,265 (95%)	566 (93%)	699 (96%)
bt_dose_rate			
HDR	765 (57%)	318 (52%)	447 (61%)
PDR	571 (43%)	289 (48%)	282 (39%)
ctv-hr-volume	29 (21, 41)	30 (22, 42)	28 (19, 41)
total_hrctv_d90	90 (85, 94)	91 (87, 95)	88 (83, 93)
total_gtv_d98	99 (89, 111)	102 (94, 113)	96 (87, 110)
total_irctv_d98	63.3 (61.1, 65.9)	64.4 (62.0, 66.8)	62.6 (60.3, 65.3)
total_bladder_d2cc	76 (69, 83)	74 (69, 82)	78 (70, 84)
total_icru_bladder	65 (57, 76)	65 (56, 74)	66 (57, 78)
total_rectum_d2cc	62 (57, 68)	62 (57, 66)	63 (58, 69)
total_icru_rectum	65 (60, 71)	64 (60, 68)	66 (60, 73)
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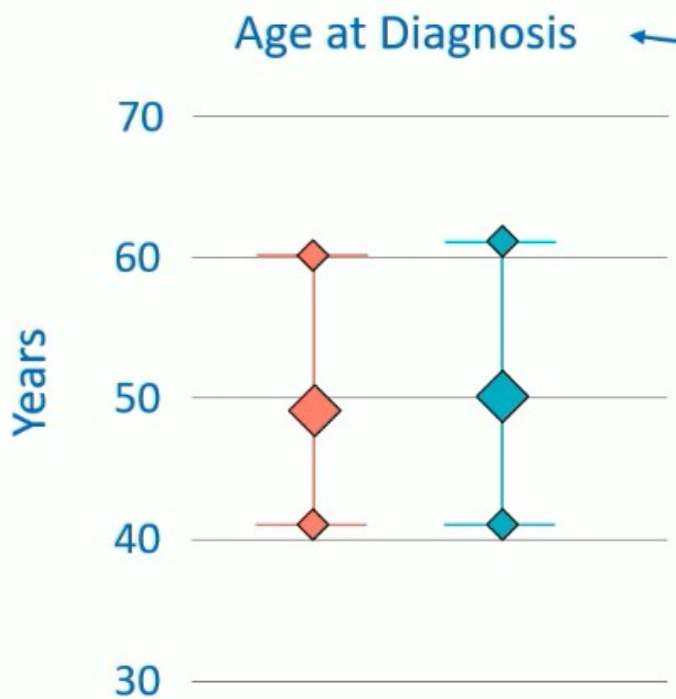
Results

EMBRACE-I Original Cohort *2021 (N=1341)*

Vs.

EMBRACE-I Extended FU Cohort *2024 (N=609)*



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Results

EMBRACE-I Original Cohort *2021 (N=1341)*

Vs.

EMBRACE-I Extended FU Cohort *2024 (N=609)*

Performance Status: no significant difference

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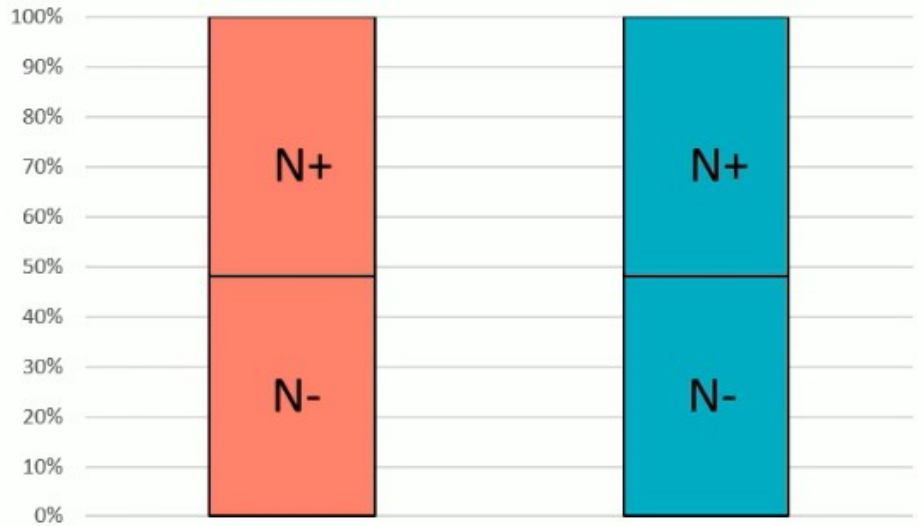
Results

EMBRACE-I Original Cohort *2021 (N=1341)*

Vs.

EMBRACE-I Extended FU Cohort *2024 (N=609)*

Nodal status



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Results

EMBRACE-I Original Cohort *2021 (N=1341)*

Vs.

EMBRACE-I Extended FU Cohort *2024 (N=609)*

DVH Parameters: no significant difference

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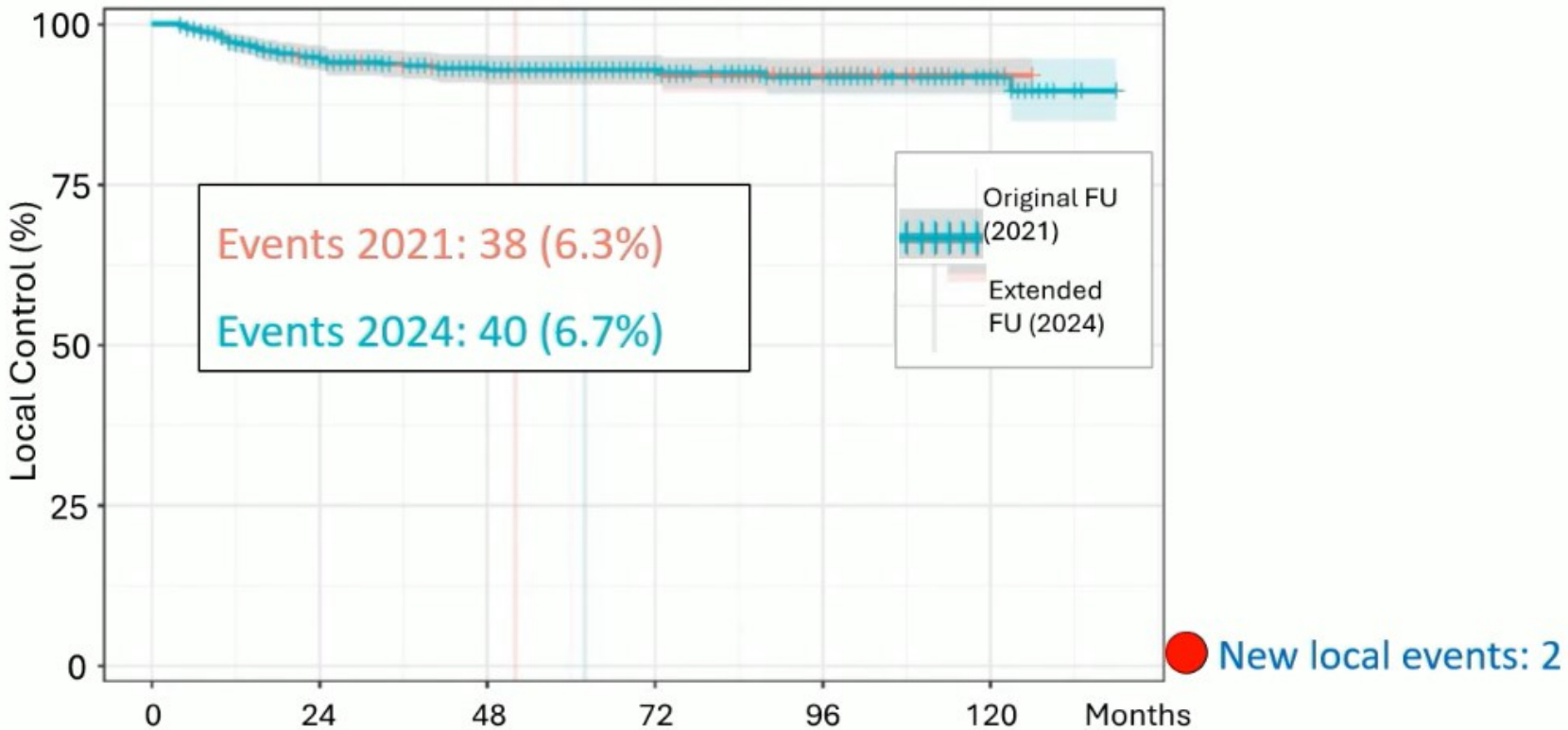
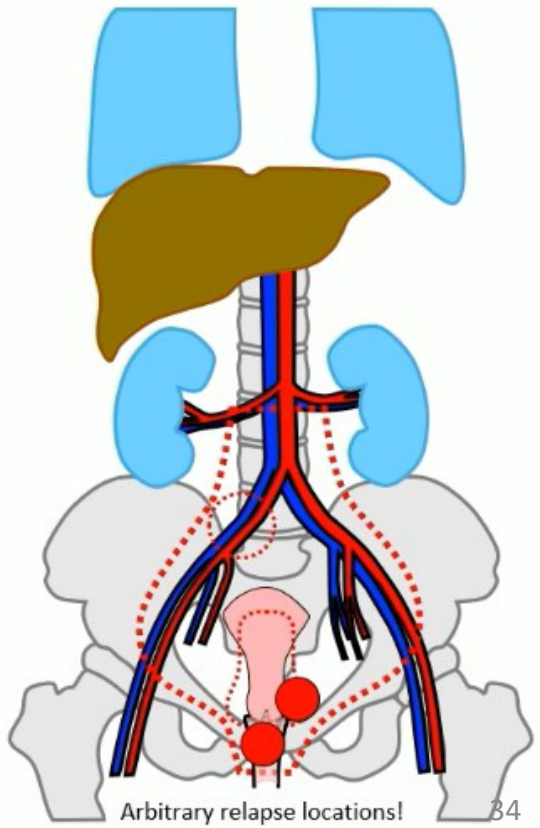
Results

	Median FU (months)	Actuarial Rate	Local Control	Nodal Control	Systemic Control	Overall Survival
EMBRACE-I Extended FU *(N=609)*	84 / 108	@ 5 years	92%			
		@ 10 years	92%			



New local events: 2



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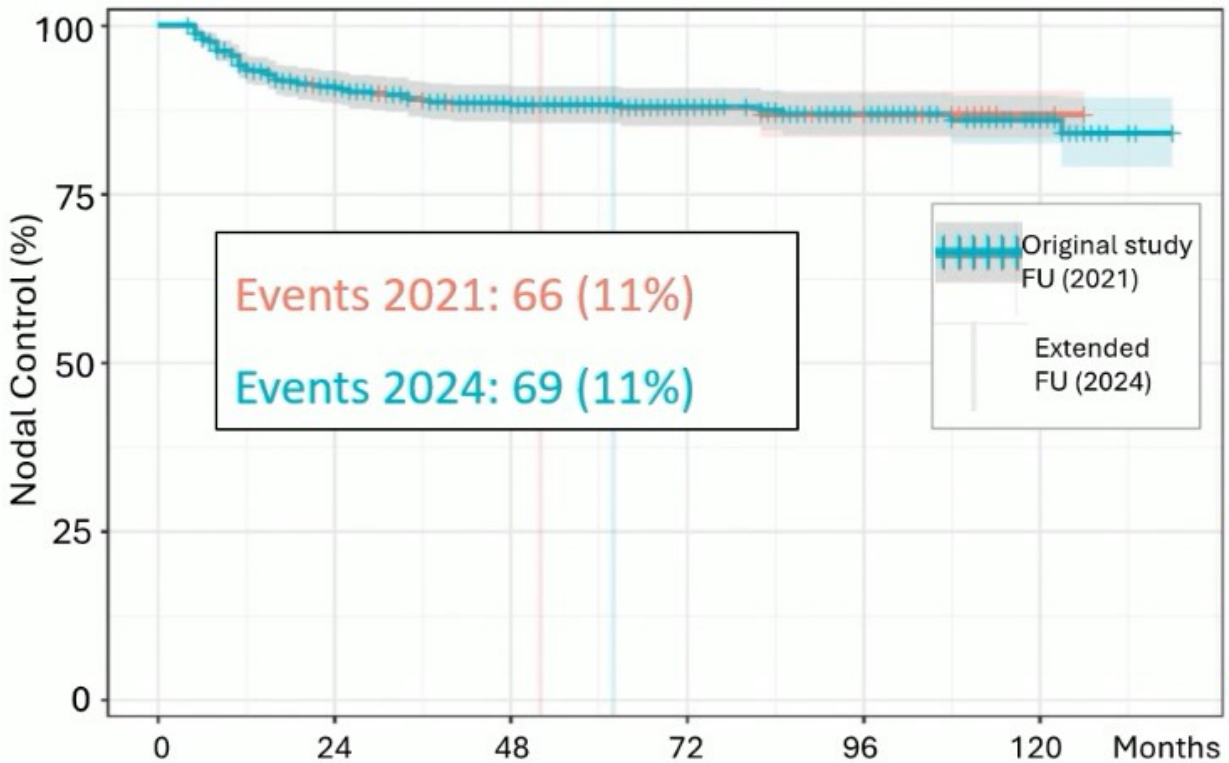
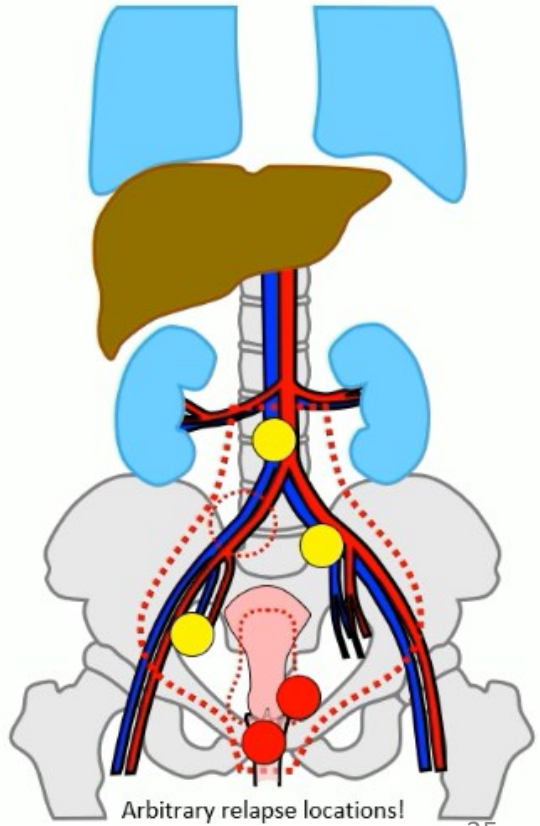


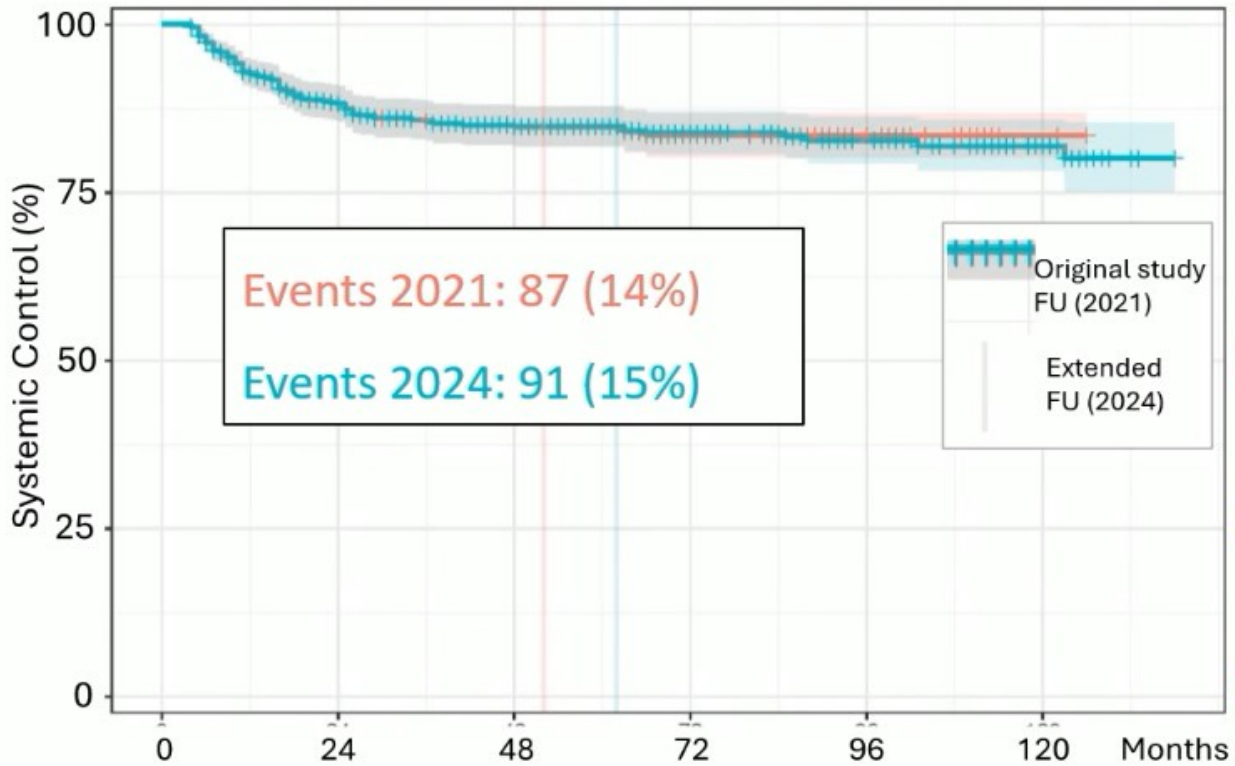
New nodal events: 3

New local events: 2



Results

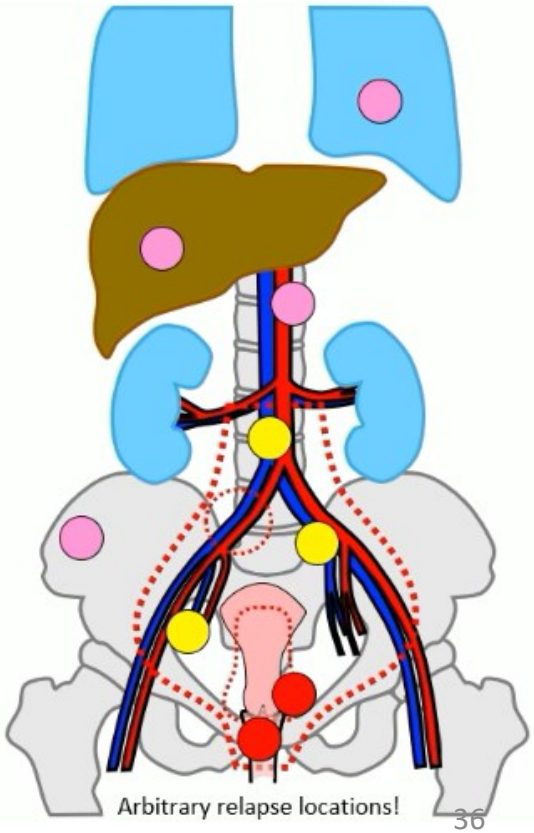
	Median FU (months)	Actuarial Rate	Local Control	Nodal Control	Systemic Control	Overall Survival
EMBRACE-I Extended FU *(N=609)*	84 / 108	@ 5 years	92%	87%	83%	
		@ 10 years	92%	86%	82%	



New systemic events: 4

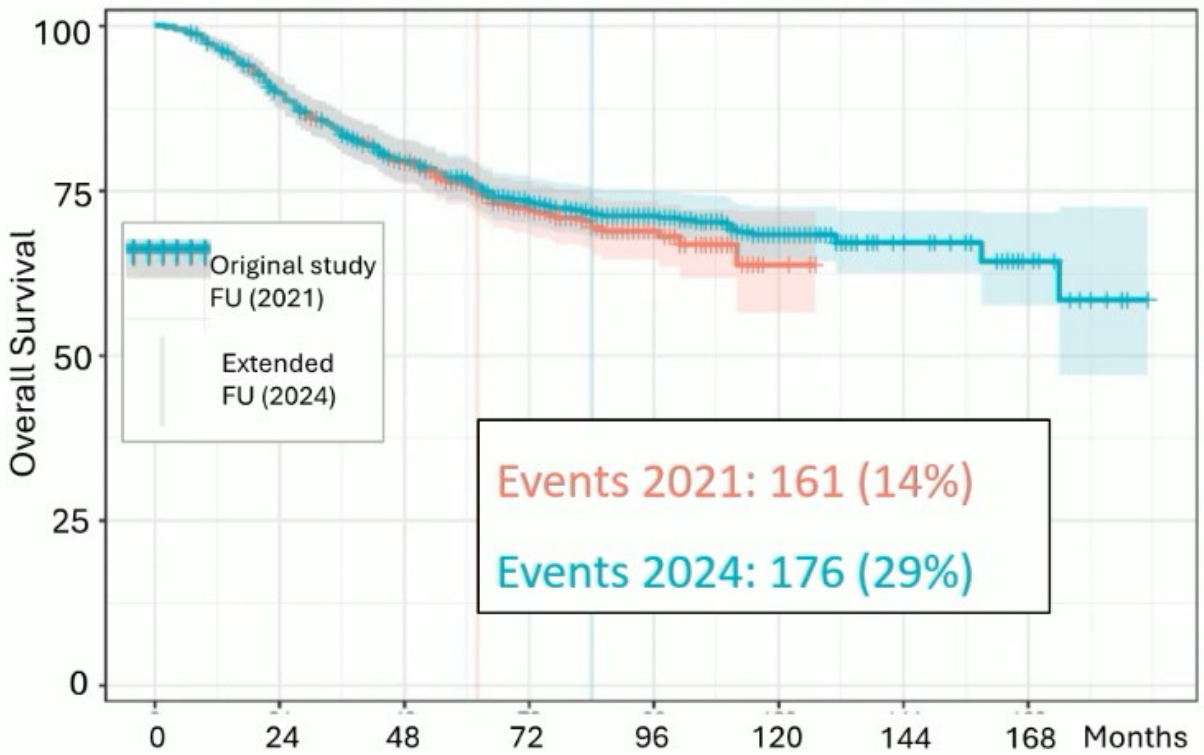
New nodal events: 3

New local events: 2

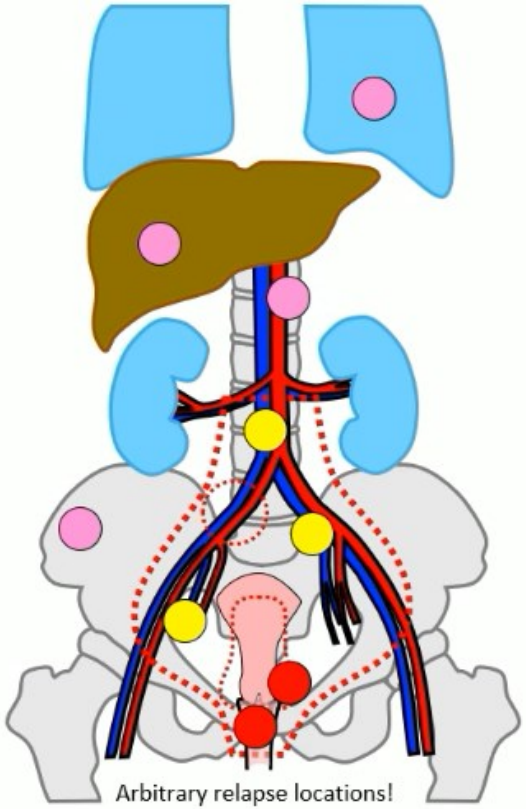


Results

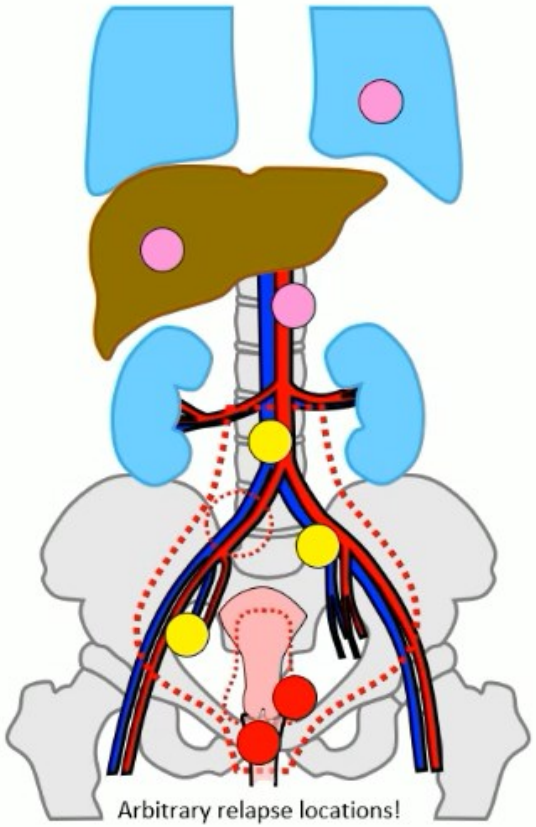
	Median FU (months)	Actuarial Rate	Local Control	Nodal Control	Systemic Control	Overall Survival
EMBRACE-I Extended FU *(N=609)*	84 / 108	@ 5 years	92%	87%	83%	74%
		@ 10 years	92%	86%	82%	68%



- New deaths 15
- New systemic events: 4
- New nodal events: 3
- New local events: 2



Conclusions



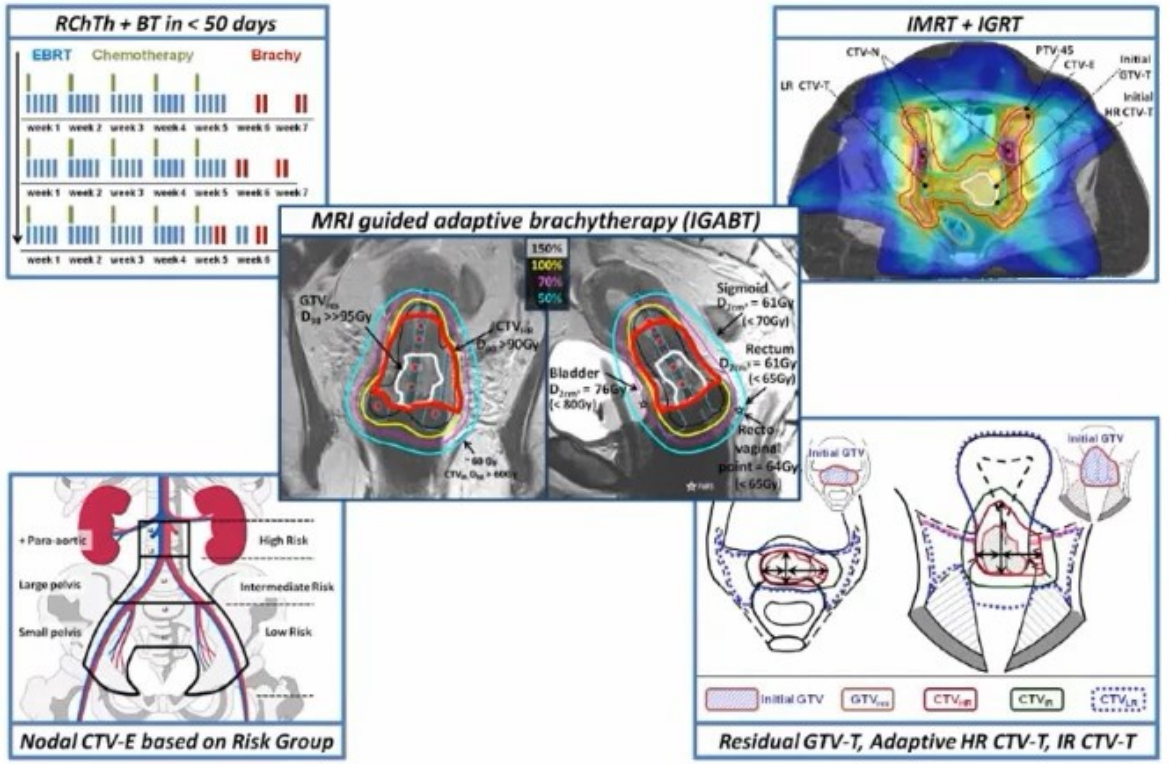
- **EMBRACE-I ChRT with MRI-IGABT, long follow-up:**
  - Sustained survival
  - Sustained loco-regional control
  - Sustained systemic control
- **Low number of relapses beyond 5 years**
  - Extended follow up outside trials of limited value

EMBRACE-type ChRT/IGABT: gold standard for LACC

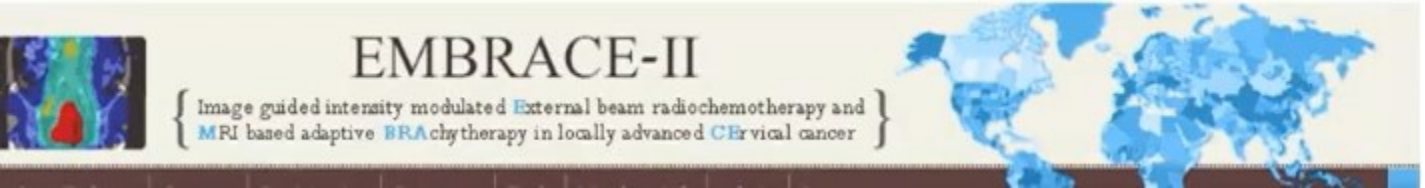
Richard Pötter, Kari Tanderup, Maximilian Schmid, Stefan Ecker, Petra Kroon, Jacob C. Lindegaard, Kjersti Bruheim, Barbara Segedin, Alina Sturdza, Henrike Westerveld, Supriya Chopra, Fleur Huang, Margit Valgma, Laura Velema, A.C. de Leeuw, Max Peters, Marianne Sanggaard-Assenholt, Nicole Eder- Nesvacil, 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

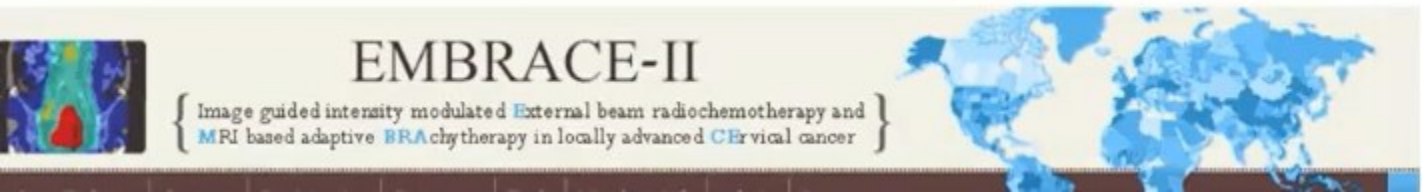


- 49 centres, 1449 patientes (1376 éligibles)
- RT externe: IMRT/VMAT/IGRT (SIB):
  pelvis: 45 Gy en 25 fr
  N+ pelviens: 55 Gy en 25 fr
  N+ LAo: 57 Gy en 25 fr
- CT hebdomadaire: Cisplat 40mg/m^2
- Curiethérapie: guidée par IRM (HDR/PDR):
  4 fr de 7 Gy (dose totale: >= 90 Gy EQD2)



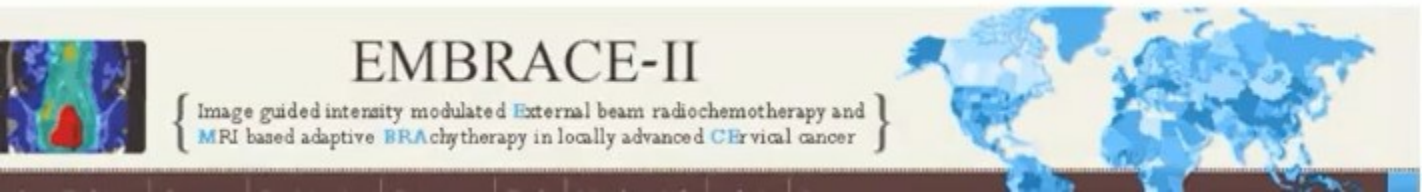
n	1376
Median age (IQR)	51 years (41, 61)
WHO performance status	PS0: 68% PS1: 30% PS2: 2%
Histology	SCC: 83% Adeno: 15% Adenosquamous: 2%
Median GTV-T-init (IQR)	37 cm^3 (19, 67)
Median GTV-T-res (IQR)	5 cm^3 (3, 9)

T- stage TNM_{2013}		
	T1b	185 (13.5%)
	T2a	75 (5.5%)
	T2b	902 (65,6%)
	T3a	19 (1.4%)
	T3b	156 (11.3%)
	T4	35 (2.5%)
N- stage TNM_{2013}		
	N0	612 (45%)
	N1	758 (55%)
	M1(PAO)	118 (8,6%)

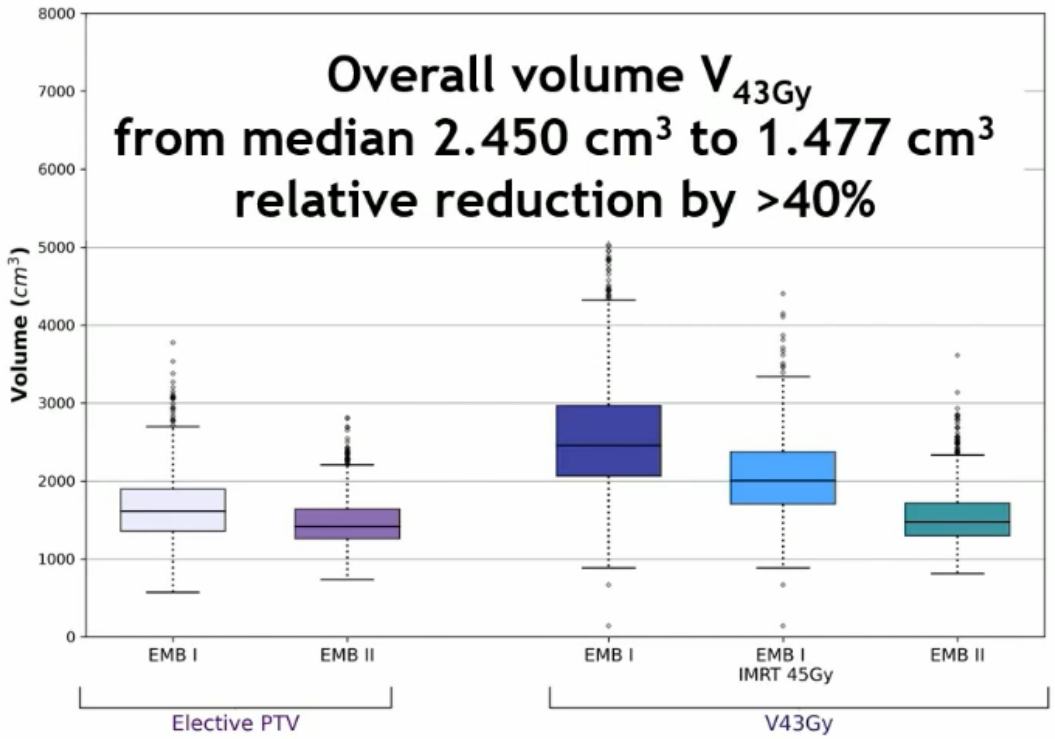


EBRT/IGRT/IMRT*	
Target volume*	Small pelvis: 3% Large pelvis (LP): 66% Large pelvis + lowPAO: 27%
Median elective dose Median V_{43Gy} (cm^3)* Conformity Index (CI)*	45 Gy, 1.8 Gy/fraction LP: 1409, LP+low PAO 1758 LP: 1.03, LP+lowPAO: 1.05
Median LN-SIB dose* Median PTV-N*	56/58 Gy 2.3 Gy/fraction 39 cm^3
Chemotherapy	
Concomitant cisplatin	97%
≥ 5 cycles	74%

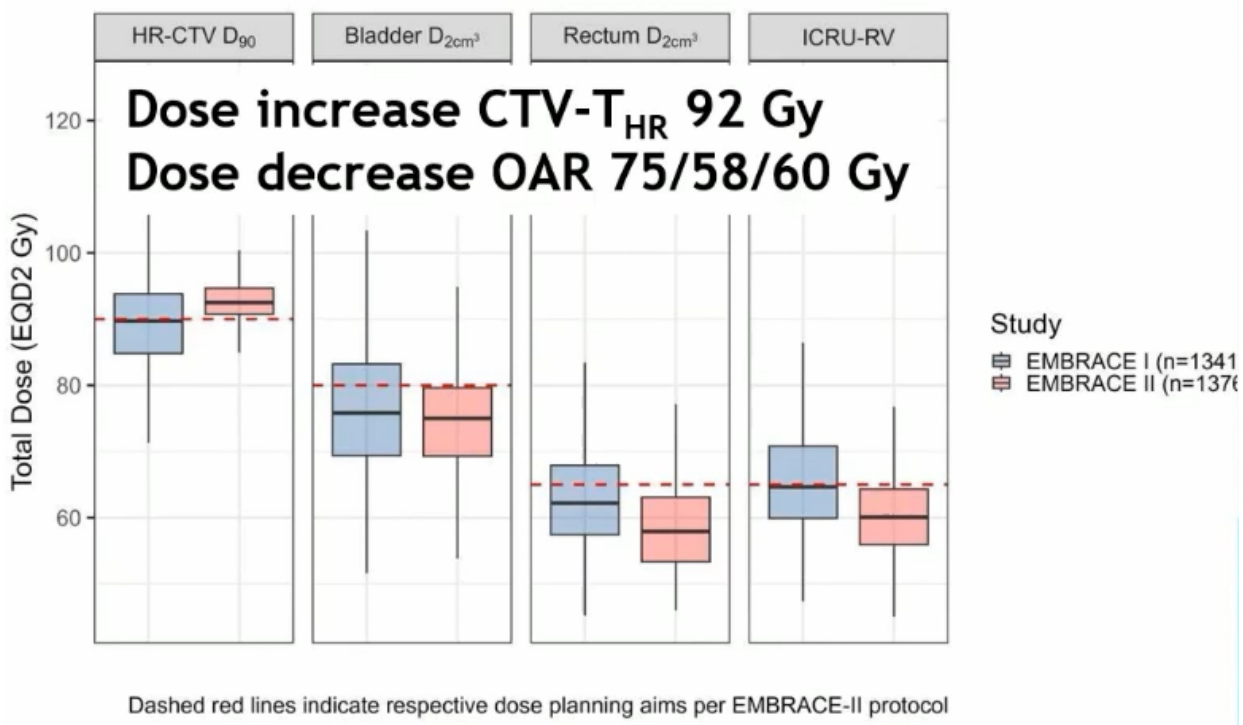
MR-IGABT**	
HDR/PDR	70%/30%
Comb. Intracavit./interstitial**	74%
Median D90: CTV-T-HR (IQR)**	92 Gy (91, 95)
Median D2cc: bladder**	75 Gy (69, 80)
Median D2cc: rectum**	58 Gy (53, 63)
Median D2cc: sigmoid**	62 Gy (57, 67)
Median D2cc: bowel**	58 Gy (50, 66)
Median recto-vaginal point**	60 Gy (56, 64)



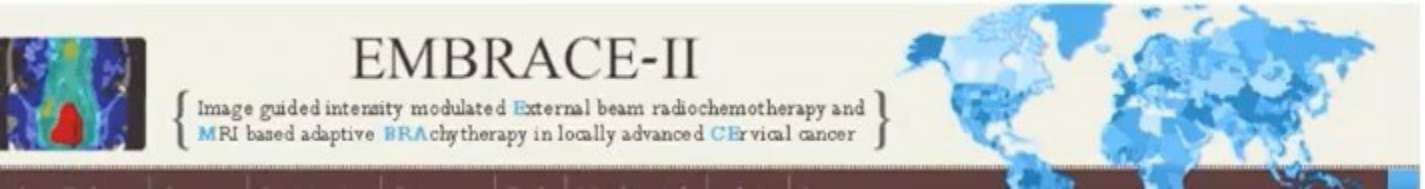
Amélioration des doses et des volumes: de l'EMBRACE I à L'EMBRACE II

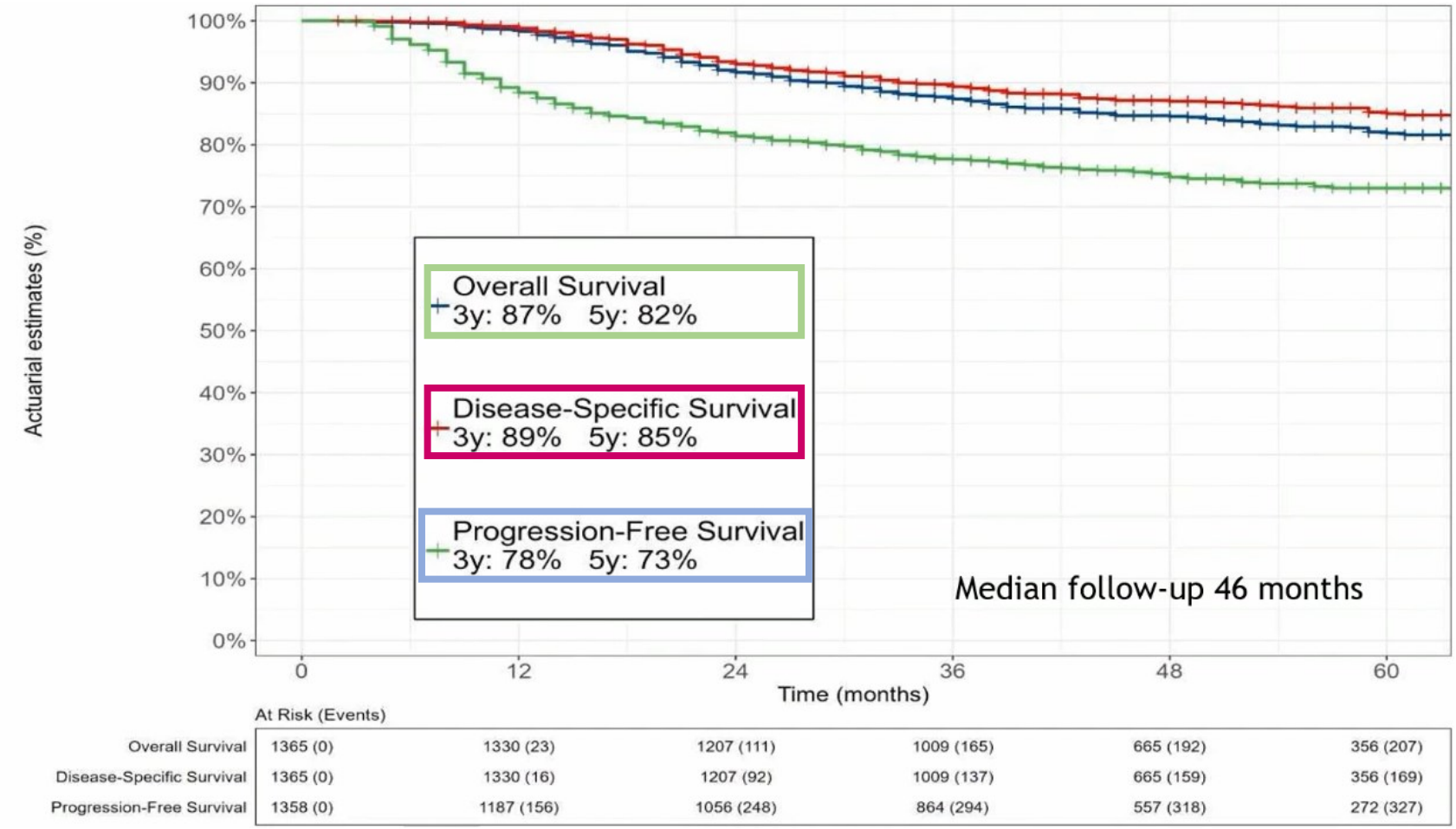


IMRT/IGRT: Aim for high conformality:
elective PTV-E_{45Gy}: V95% ~ 95%



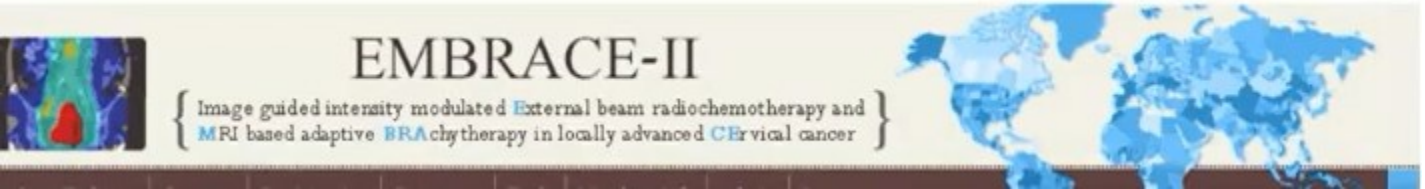
MR-IGABT: multi-parametric dose/volume
prescription for CTV-T_{HR} and OARs

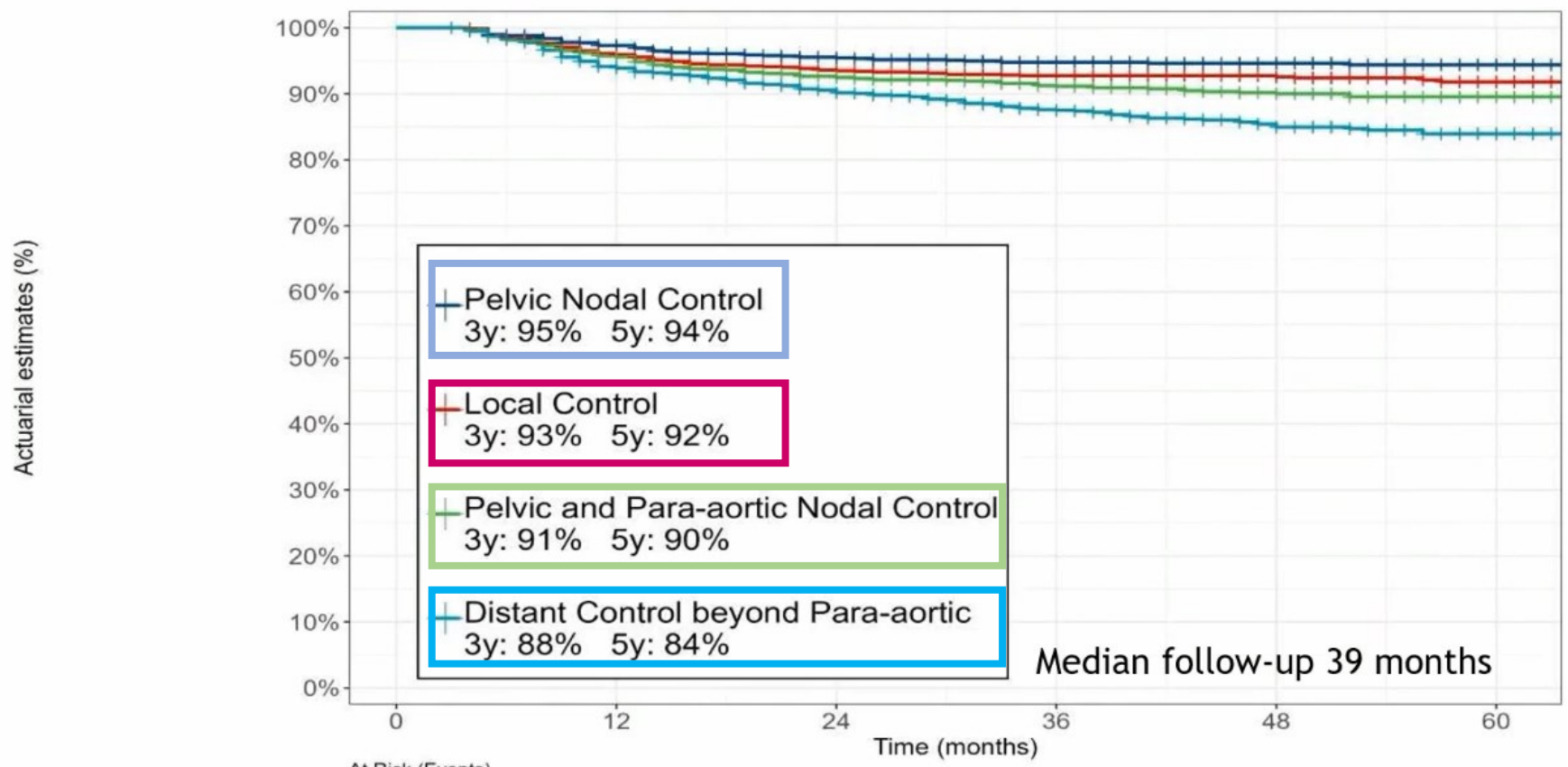




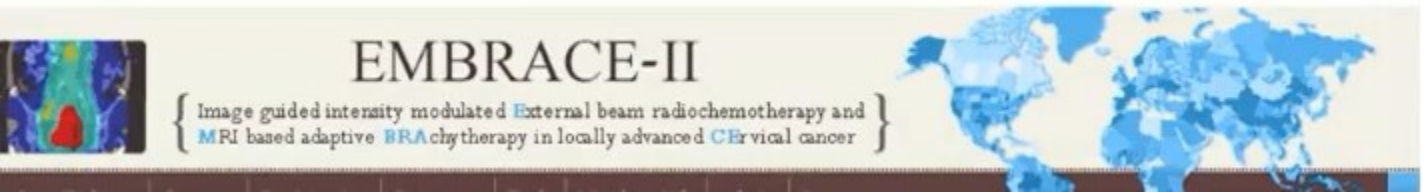
At Risk (Events)

Overall Survival	1365 (0)	1330 (23)	1207 (111)	1009 (165)	665 (192)	356 (207)
Disease-Specific Survival	1365 (0)	1330 (16)	1207 (92)	1009 (137)	665 (159)	356 (169)
Progression-Free Survival	1358 (0)	1187 (156)	1056 (248)	864 (294)	557 (318)	272 (327)



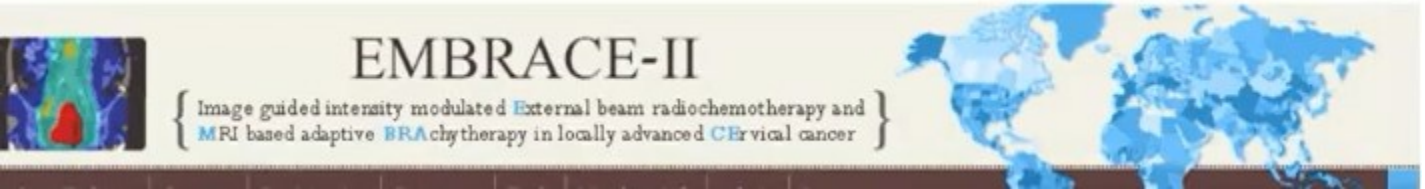


At Risk (Events)						
Pelvic Nodal Control	1358 (0)	1187 (35)	1056 (57)	864 (64)	557 (65)	272 (66)
Local Control	1358 (0)	1187 (53)	1056 (82)	864 (90)	557 (91)	272 (94)
Pelvic and Para-aortic Nodal Control	1358 (0)	1187 (58)	1056 (95)	864 (109)	557 (117)	272 (119)
Distant Control beyond Para-aortic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



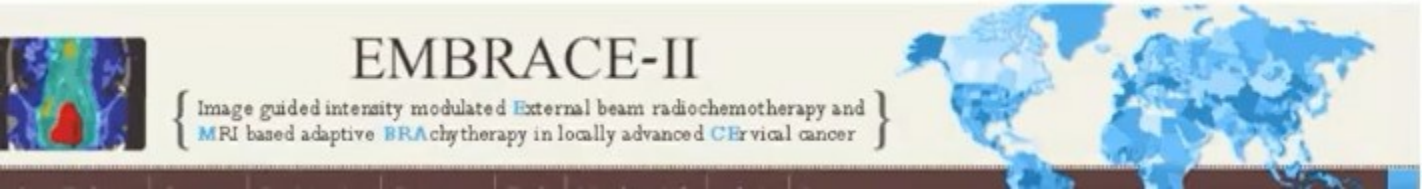
EMBRACE I vs hypothèses de L'EMBRACE II vs EMBRACE II: Amélioration des résultats cliniques

	EMBRACE-I	EMBRACE-II	
	Results overall 3y	Hypotheses overall 3y	**Results overall 3y**
n Patients	1341	-	**1376**
Median Follow-up (months)	51	-	**39**
Local Control	92%	93%	**93%**
Pelvic Control	88%	90%	**89%**
Pelvic nodal Control	93%	95%	**95%**
Para-aortic nodal Control	92%	-	**94%**
Pelvic and PAO nodal Control	88%	90%	**91%**
Local and pelvic and para-aortic control	83% (crude)	-	**86%**
Distant control beyond PAOortic	86%	86%	**88%**



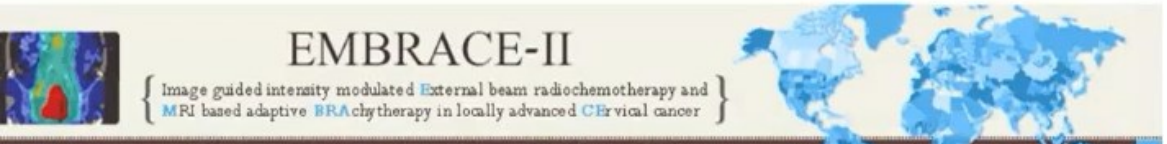
EMBRACE I vs hypothèses de L'EMBRACE II vs EMBRACE II: Amélioration des résultats cliniques

	EMBRACE-I	EMBRACE-II	
	Results overall 3y	Hypotheses overall 3y	**Results overall 3y**
n Patients	1341	-	**1376**
Disease Control	76%	-	**80%**
Disease-Specific Survival	84%	85%	**89%**
Disease-Free Survival (Progression-Free Survival)	72%	-	**78%**
Overall Survival	82%	81%	**87%**
Late GI/GU/Vag G4 morbidity	4%	-	**1%**
Late morbidity G5	12 pats.	-	**2 pats.**



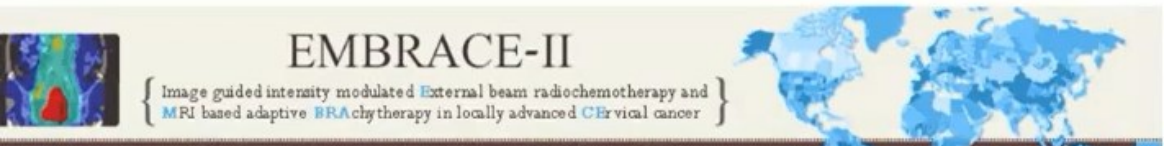
EMBRACE II:
Excellents résultats cliniques même pour les groupes à haut risque

	EMBRACE-II	
	Results overall 3y	Results T3/T4 + T1/T2N1+M1PAO 3y
n Patients	1376	846
Median Follow-up (months)	39	39
Local Control	93%	92%
Pelvic Control	89%	87%
Pelvic nodal Control	95%	93%
Para-aortic nodal Control	94%	92%
Pelvic and PAO nodal Control	91%	88%
Local and pelvic and para-aortic control	86%	83%
Distant control beyond PAOortic	88%	85%
Disease Control	80%	75%
Disease-Specific Survival	89%	86%
Disease-Free Survival (Progression-Free Survival)	78%	73%
Overall Survival	87%	84%



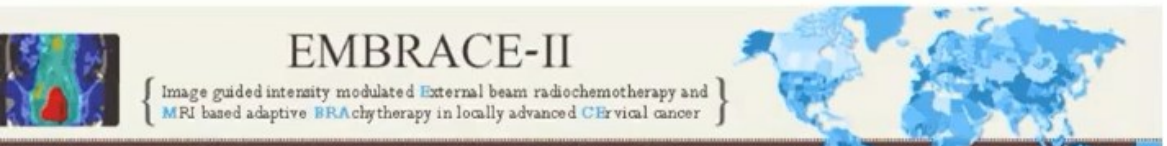
EMBRACE II:
Excellents résultats cliniques en termes de toxicités G<= 3

	events	patients	% (crude)
≥ total G3	170	116	8.9%
G3	159	106	8.1
G4	9	8	<1%
G5	-	2	< 0.2%
≥ G3 urinary	51	37	2.8%
≥ G3 gastrointestinal	65	49	3.7%
≥ G3 vagina	43	42	3.2%
Fistula		11 (9 G3, 2 G4)	0.8%



EMBRACE I vs EMBRACE II: Nette amélioration des toxicités G<= 3

Embrace I* vs Embrace II (n)	Reduction of morbidity by…
total G3 (events)	42%
Diarrhea (9), bleeding (GI) (8)	>50%
Cystitis (5), urinary frequency (9)	>50%
Vaginal stenosis (29)	20%
Fistula (11)	68%
Total G4 (patients)	>80%
Total G5 (patients)	>80%



EMBRACE II: NEW STANDARD of CARE for LOCALLY ADVANCED CERVIX CANCER

- **Using advanced radiation therapy technology**

  EBRT: IGRT/IMRT 45 Gy with limited PTV margins (5mm), risk adapted target selection (±low PAO)

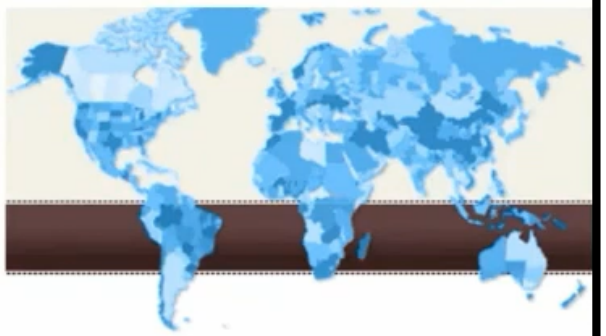
  multi-parametric highly conformal treatment planning: CI: <1.05

  LN-SIB (57 Gy) with limited margins (5mm), CovP Plannning

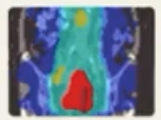
  BT: MR-IGABT with IC/IS technique, adaptive target volumes

  multi-parametric protocol based treatment planning

  balancing CTV_{HR} $D_{90\%}$ ≥ 90 Gy and OAR_{2cm3} <65-75Gy



- **Using concomitant cis-Platin** (5-6 cycles)
- **Limiting overall treatment time** (42-45 days)



EMBRACE-II

{ Image guided intensity modulated External beam radiochemotherapy and MRI based adaptive BRAchytherapy in locally advanced CErvical cancer }

Improving disease control and survival, decreasing late G3-G5 morbidity