Gynaecologic Cancer Intergroup

Cervix Cancer Research Network

INTERLACE

A phase III multicentre trial of weekly induction chemotherapy followed by standard chemoradiation versus standard chemoradiation alone in patients with locally advanced cervical cancer

Chief Investigator - Dr Mary McCormack

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LACC and Survival 2018

- 1999- NCI announcement---incorporation of CHEMO—30-50% reduction in risk of dying
- Meta-analysis 2008-----CRT improved outcome 5yr OS 66% (RT 60%)
- Advances in Radiotherapy—esp Brachytherapy -RetroEMBRACE

Additional Chemotherapy in front line setting

- Intensification CRT [1] (Gem/Cispl) & adjuvant chemo (GC x 2)
  - 9% improvement PFS at 3 years (65% → 74%)
  - significant toxicity & no OS data

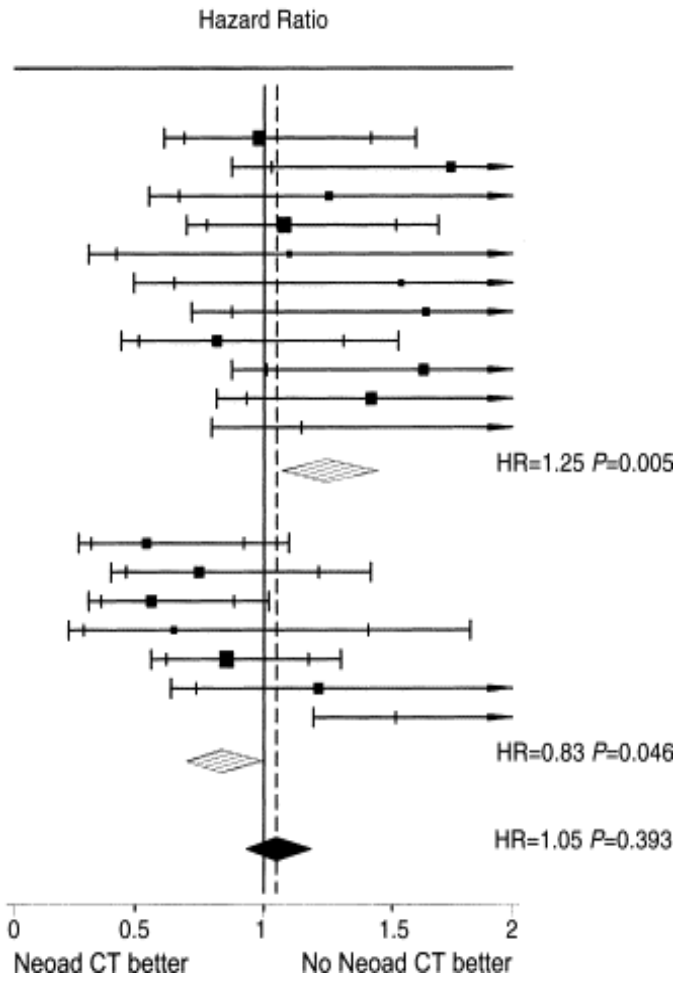
- OUTBACK –CRT v CRT + 4 cycles adjuvant Carbo/Paclitaxel
  - recently completed accrual
  - 915 patients/ 325 sites

Role of additional chemotherapy remains to be defined

1 Duenas-Gonzalez JCO 2011

Neoadjuvant (induction) chemotherapy & RT

Trial	Neoad CT (no. events/no. entered)	No Neoad CT	O-E	Variance
>14 day cycles				
Chauvergne, 1993	57/92	54/90	−0.47	27.66
Souhami, 1991	29/48	31/55	7.64	13.64
Tattersall, 1992	20/34	18/37	2.17	9.41
Herod, 2001	68/89	62/88	2.60	32.39
Cardenas, 1991	7/13	9/18	0.37	3.84
Cardenas, 1993	12/14	8/16	2.16	4.91
Chiara, 1994	22/32	16/32	4.68	9.33
Sundfor, 1996	31/48	35/48	−3.41	16.40
CCSG AOCOA	38/129	28/131	8.08	16.31
Kumar, 1998	49/88	34/85	7.43	20.73
LGOG	9/15	2/12	3.61	2.73
Sub-total	342/602	297/612	34.85	157.36
⩽14 day cycles				
Sardi, 1997	19/104	32/106	−7.97	12.69
Sardi, 1998	30/73	33/74	−4.61	15.56
Sardi, 1996	34/54	41/54	−10.61	17.89
PMB	9/16	15/19	−2.68	5.94
Symonds, 2000	68/105	76/110	−5.86	35.84
Leborgne, 1997	32/48	28/49	2.98	14.94
MRC CeCa	19/24	9/24	7.86	6.64
Sub-total	211/424	234/436	−20.89	109.48
Total	553/1026	531/1048	13.96	266.85



- >1000 Pts in 18 published studies
- Small numbers/ plethora regimens /most failed to show a benefit
- Suggestion of benefit with short cycle schedules….

Induction chemo- new approach

- Reduce cycle length --- **weekly** treatment
- Incorporate **taxane** and retain platinum
- **Eliminate delay** between chemotherapy and definitive CRT
- Balance need for systemic treatment with **tolerability** and ease of delivery without significantly delaying definitive treatment.

CX II - phase 2 single arm feasibility study

Weekly Paclitaxel (80mg/m^2)

&

Carboplatin (AUC2)

Weeks 1-6

Radical ChemoRT weeks 7-13

(cisplatin 40 mg/m^2)

BJC
British Journal of Cancer (2013) 108, 2464–2469 | doi: 10.1038/bjc.2013.230

Keywords: neoadjuvant chemotherapy; locally advanced; cervical cancer

A phase II study of weekly neoadjuvant chemotherapy followed by radical chemoradiation for locally advanced cervical cancer

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- Dose –dense chemo delivered before CRT is feasible
- Toxicity is manageable
- Patients completed RT on time
- No evidence of detrimental effect on outcome

Progression free and Overall survival

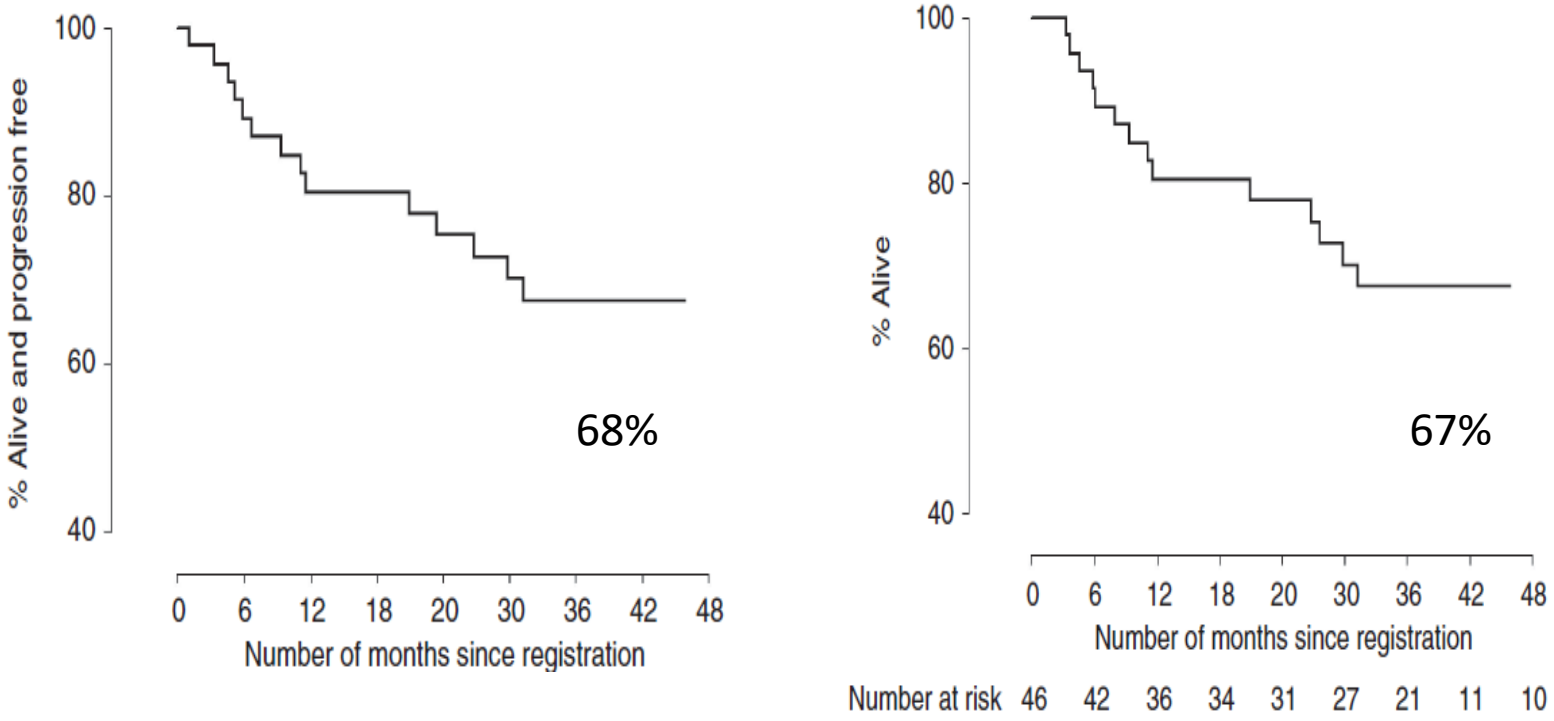

Figure 1. Kaplan–Meier plots for progression-free survival (PFS; upper) and overall survival (OS; lower) for the 46 patients in the study. The PFS and OS rates are the same for 3 and 5 years (68% and 67%) as there were no PFS or OS events between 3 and 5 years.

- 70% PR/CR to NACT at end wk6
- 85% RR at 12/52 post CRT

Br J Cancer 2013 ,108

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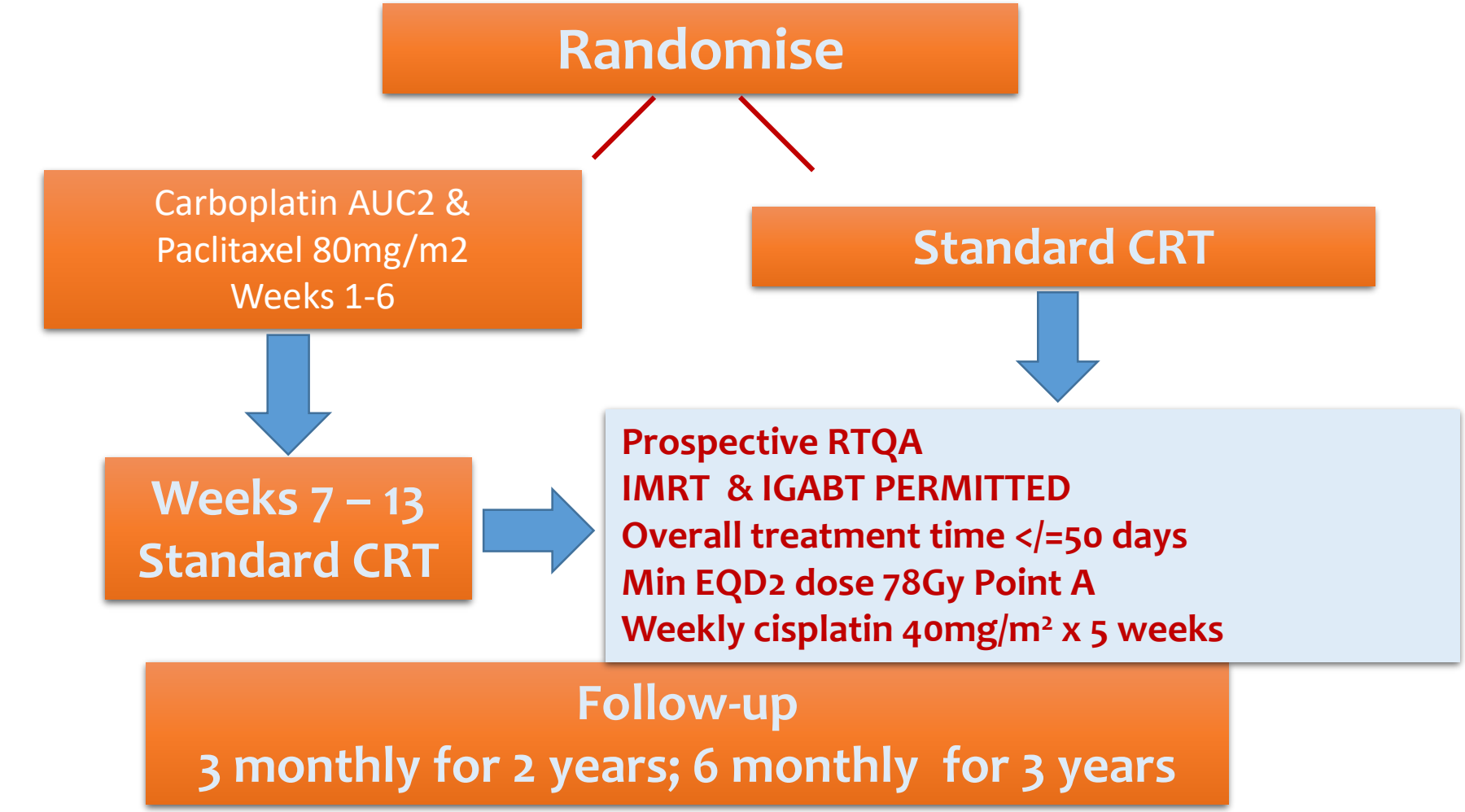

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Inclusion criteria

- FIGO 1b1 node positive
- FIGO Ib2- IVa
- SCC, Adeno, Adenosq
- Adequate renal/ liver/BM
- Documented HIV neg (high risk countries)

Exclusion criteria

- Involvement of lower 1/3 vagina
- Previous pelvic malignancy
- Prior history Crohn's/ UC
- Hydronephrosis-unless relieved by stenting/ nephrostomy except if non functioning kidney
- Enlarged (>15mm CT/MRI) lymph nodes above aortic bifurcation

Stratification

- FIGO stage
- Node status – positive / negative
- Squamous v non squamous histology
- Tumour Volume
- Institution
- IMRT V no IMRT

Endpoints & Statistics

- Primary endpoint is OS
- Secondary endpoints: PFS/ adverse events/ QOL/ patterns of relapse
- 80% power to detect a HR of 0.70
- Recruitment target 500

Recruitment update

- 30 centres UK , Mexico City & Italy
- First centre in India now open Sarouj Gupta Kolkata (3 more in set up)
- 347/500 recruited
- 70 (20%) from INCAN Mexico

Thank You

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