

Early localised treatment of Non-muscle invasive bladder cancer

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A large, abstract graphic on the left side of the slide. It features a central, irregularly shaped area filled with a dense, textured pattern of small, dark blue and teal particles, resembling a microscopic view of cancer cells. This central area is surrounded by a thick, layered border that transitions from a light yellow-green at the top to a darker teal at the bottom. The overall shape is roughly heart-like or kidney-like, with a pointed bottom and rounded top.
A white 'X' logo on a black square background.
@achoud72

bmuc.be/bmuc2024



**11th Belgian Multidisciplinary
Meeting on Urological Cancers**

Conflicts of interest

- Research funding from CRUK, MRC, NIHR, PCUK, Elekta AB
- Honoraria from Bayer PLC, Janssen, AZ, ASTRO, ASCO, Merck, Roche
- Editor in Chief, BMJ Oncology



Recurrence is the price to pay for inadequate treatment

	Univariate			Multivariate		
	Odds ratio	95% CI	<i>p</i> value	Odds ratio	95% CI	<i>p</i> value
Tumor stage (Ta; T1)	0.50	0.31; 0.78	0.001	0.42	0.25; 0.70	0.001
Tumor grade (low; high)	0.87	0.52; 1.46	0.5			
Tumor size (<3 cm; ≥3 cm)	1.	0.69; 1.75	0.61			
Multifocality (<3; ≥3)	0.25	0.10; 0.62	0.032	1.39	0.76; 2.54	0.274
BCG induction completed	0.15	0.00; 0.38	<0.001	0.25	0.10; 0.62	0.003
BCG maintenance 1 yr completed	0.28	0.17; 0.45	<0.001	0.30	0.17; 0.53	<0.001

BCG = bacillus Calmette-Guérin; CI = confidence interval.

Recurrence is the price to pay for inadequate treatment

	Univariate		Multivariate			
	Odds ratio	95% CI	Odds ratio	95% CI	p value	
Tumor stage (Ta; T1)	0.50		0.42	0.25; 0.70	0.001	
Tumor grade (low; high)	0.46	0.25; 0.85	0.5	0.28; 0.85	0.001	
Tumor size (<3 cm; ≥3 cm)	0.69	0.69; 1.75	0.61	0.42; 0.88	0.001	
Multifocality	0.25	0.10; 0.62	0.032	0.01; 0.10	0.001	
BCG induction completed	0.15	0.00; 0.38	<0.001	0.25	0.10; 0.62	0.003
BCG maintenance 1 yr completed	0.28	0.17; 0.45	<0.001	0.30	0.17; 0.53	<0.001

We need alternative strategies...

BCG = bacillus Calmette-Guérin; CI = confidence interval.

Evidence for radiotherapy

- The old MRC trial.....
- N=210 between 1991 and 2003 – underpowered, but no difference

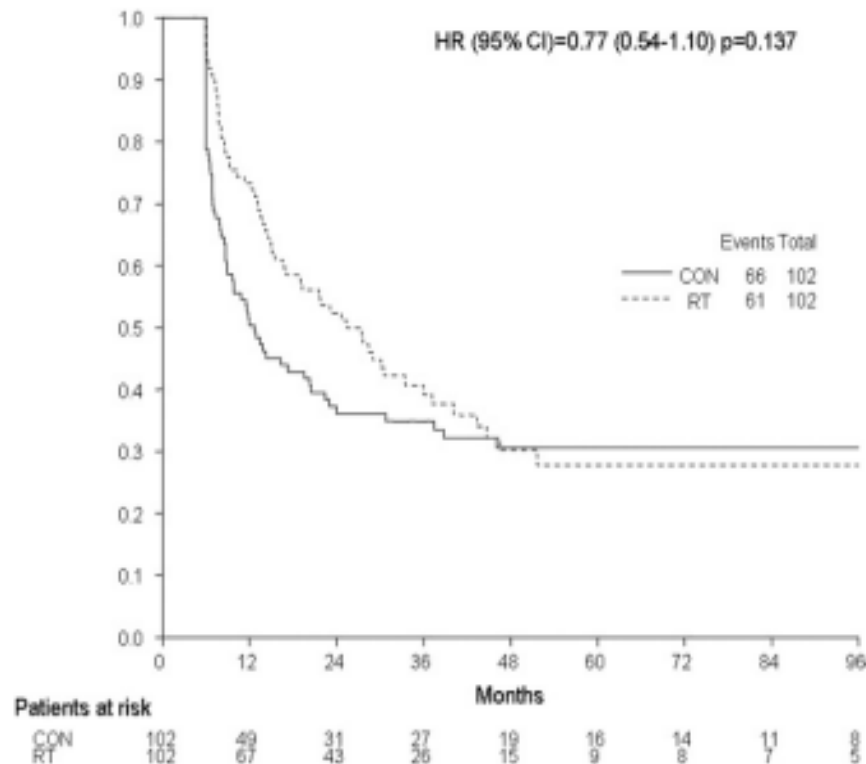


FIG. 5. Recurrence-free interval

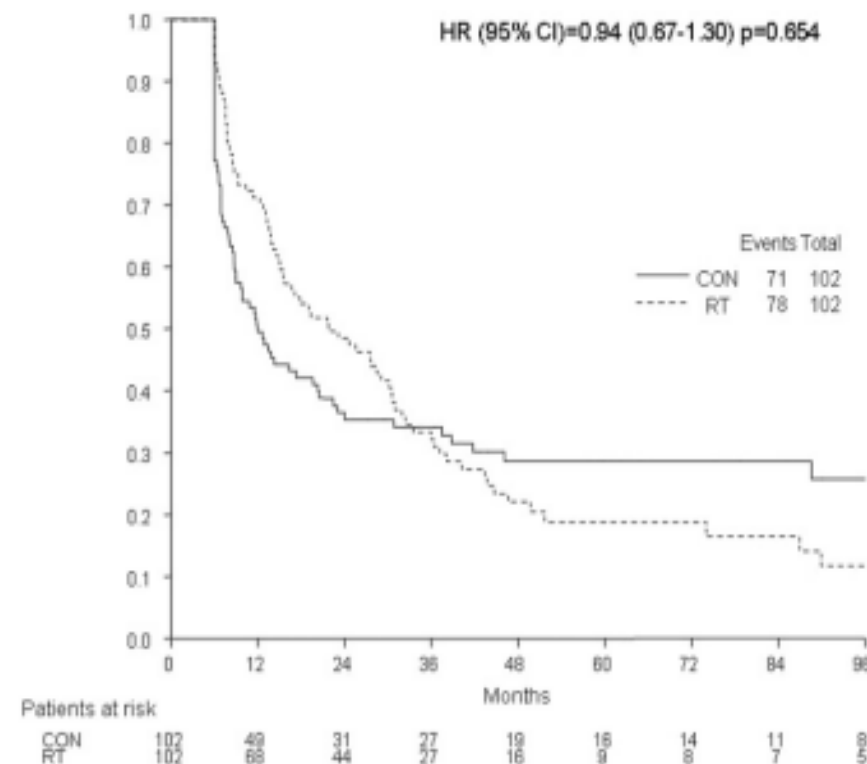


FIG. 6. Recurrence-free survival

The Hoosier Cancer Research Network GU16-243 ADAPT-BLADDER Study

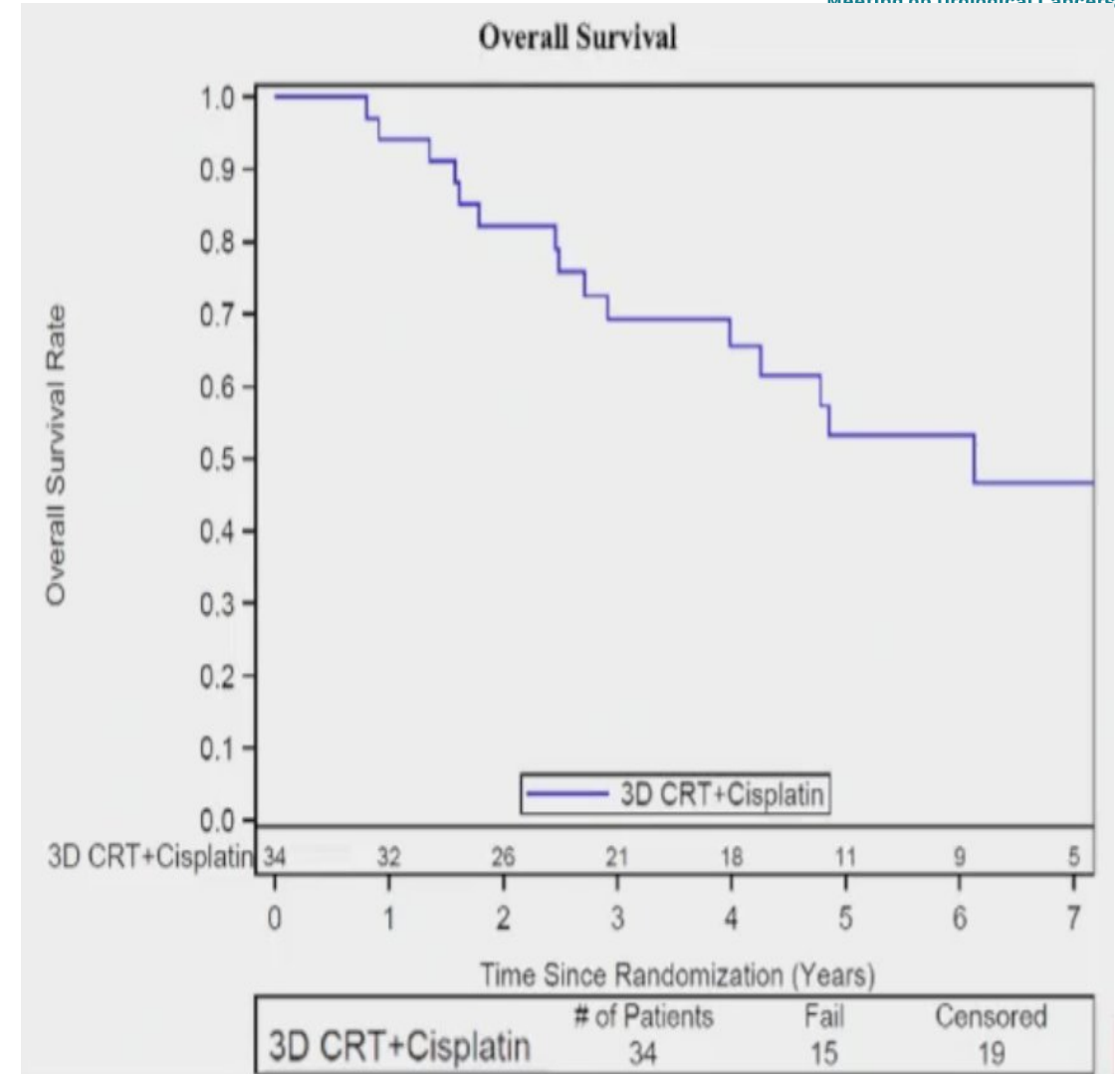
Table 4. Complete response rates at 3, 6, and 12 mo after treatment

Time point (mo)	All cohorts		Durvalumab(cohort 1)		Durvalumab + BCG (cohort 2)		Durvalumab + EBRT (cohort 3)	
	Evaluable patients	CR rate (%)	Evaluable patients	CR rate (%)	Evaluable patients	CR rate (%)	Evaluable patients	CR rate (%)
3	28	64	3	33	13	85	12	50
6	27	52	3	0	12	83	12	33
12	26	46	3	0	11	73	12	33

BCG = bacillus Calmette-Guerin; CR = complete response; EBRT = external beam radiation therapy.

Contemporary Data: RTOG 0926

- Single arm, phase II trial of TMT for recurrent, high-grade NMIBC
- 61.2 Gy / 34 # with cisplatin or MMC/5FU for radiosensitization
- 37 patients enrolled between 2009-2017
 - 3 yr freedom from cystectomy rate was 88%
 - 11 pt had local recurrence at 3 yrs



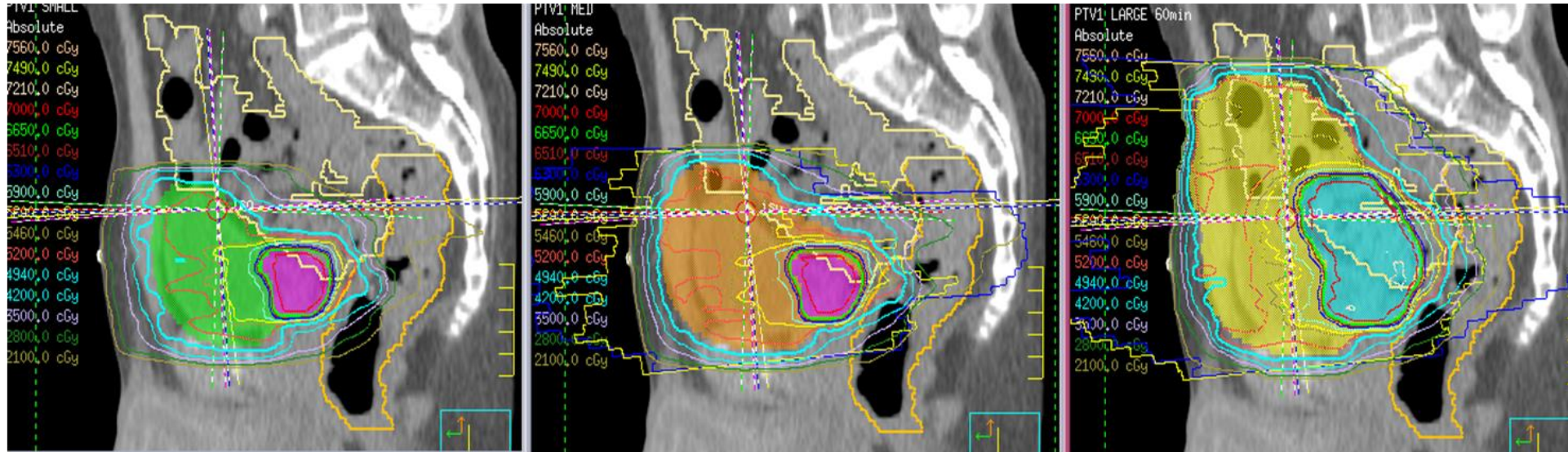
Radiotherapy has advanced since the 1990s

- Adaptive image-guided radiotherapy
- Radiosensitisation
- Hypofractionation
- And we should be better at diagnosis and pathway management...



Further advances in radiotherapy: Adaptive radiotherapy with Plan of the Day 'PoD'

Coronal planning CT scans to illustrate 3 plans for daily selection

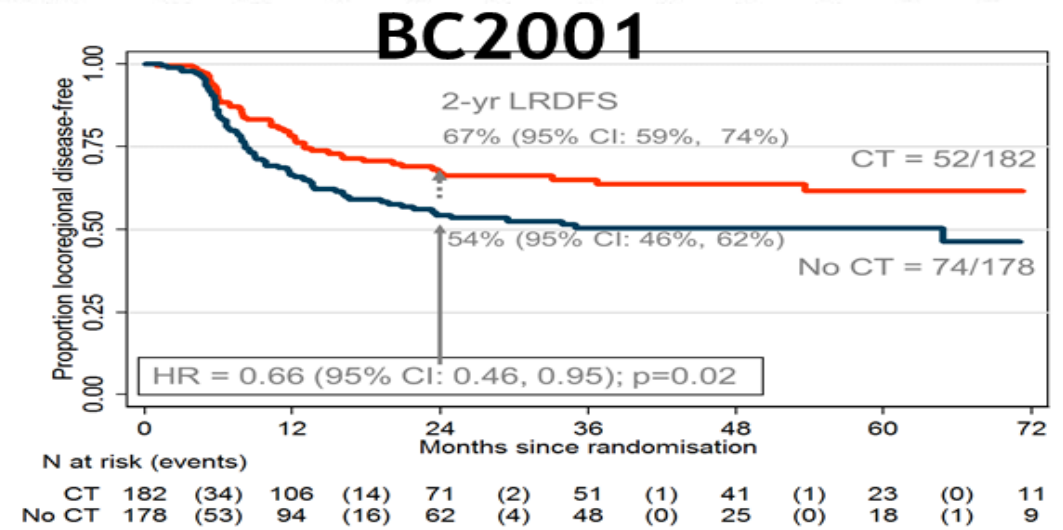
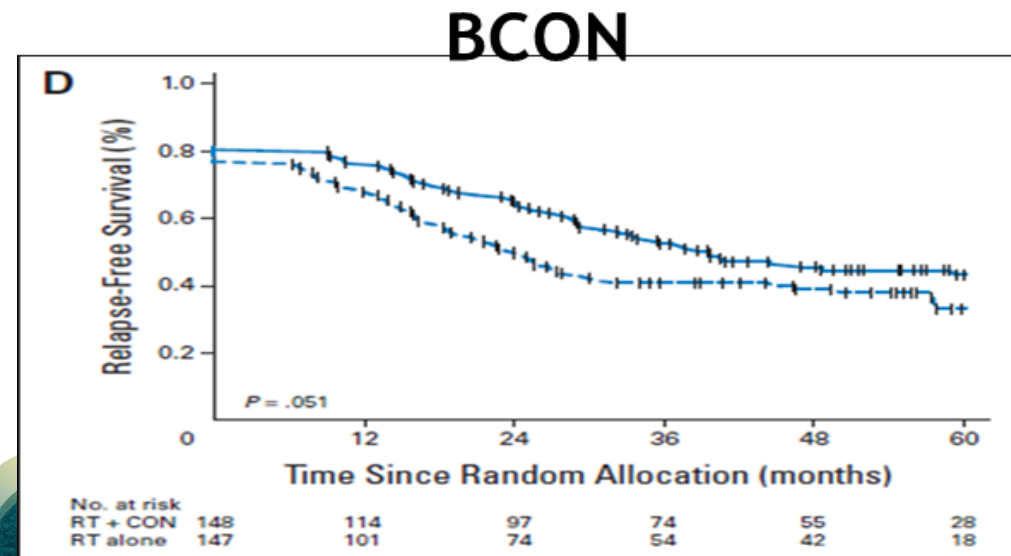
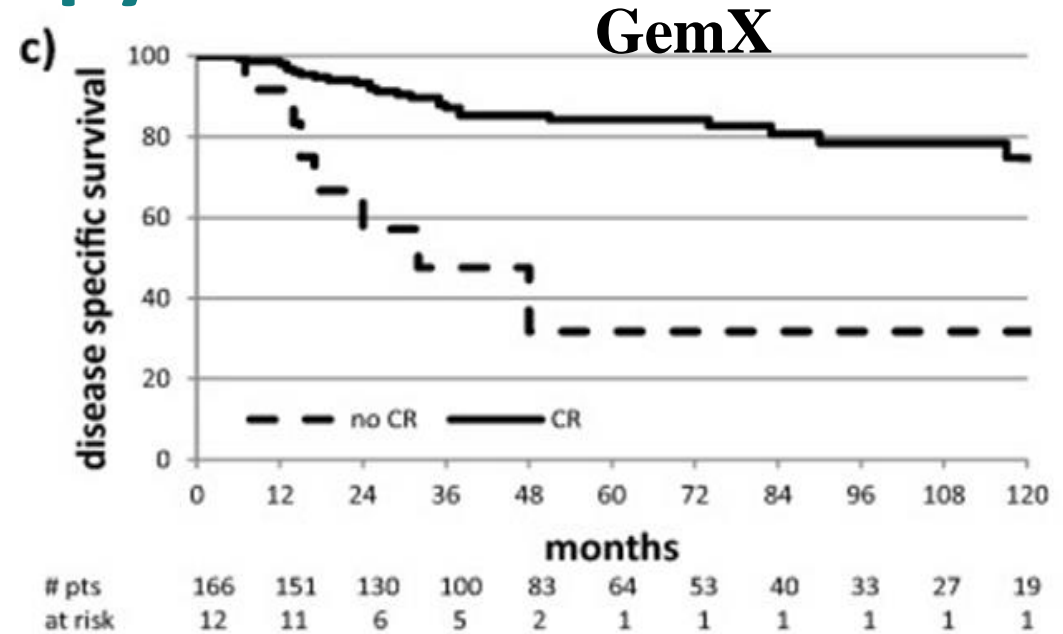
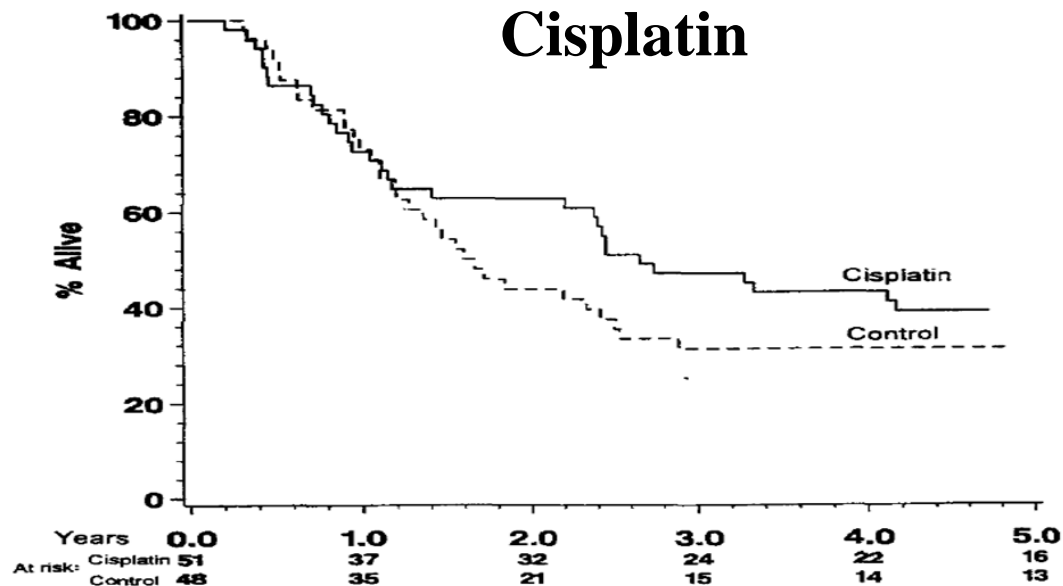


Process for Plan selection

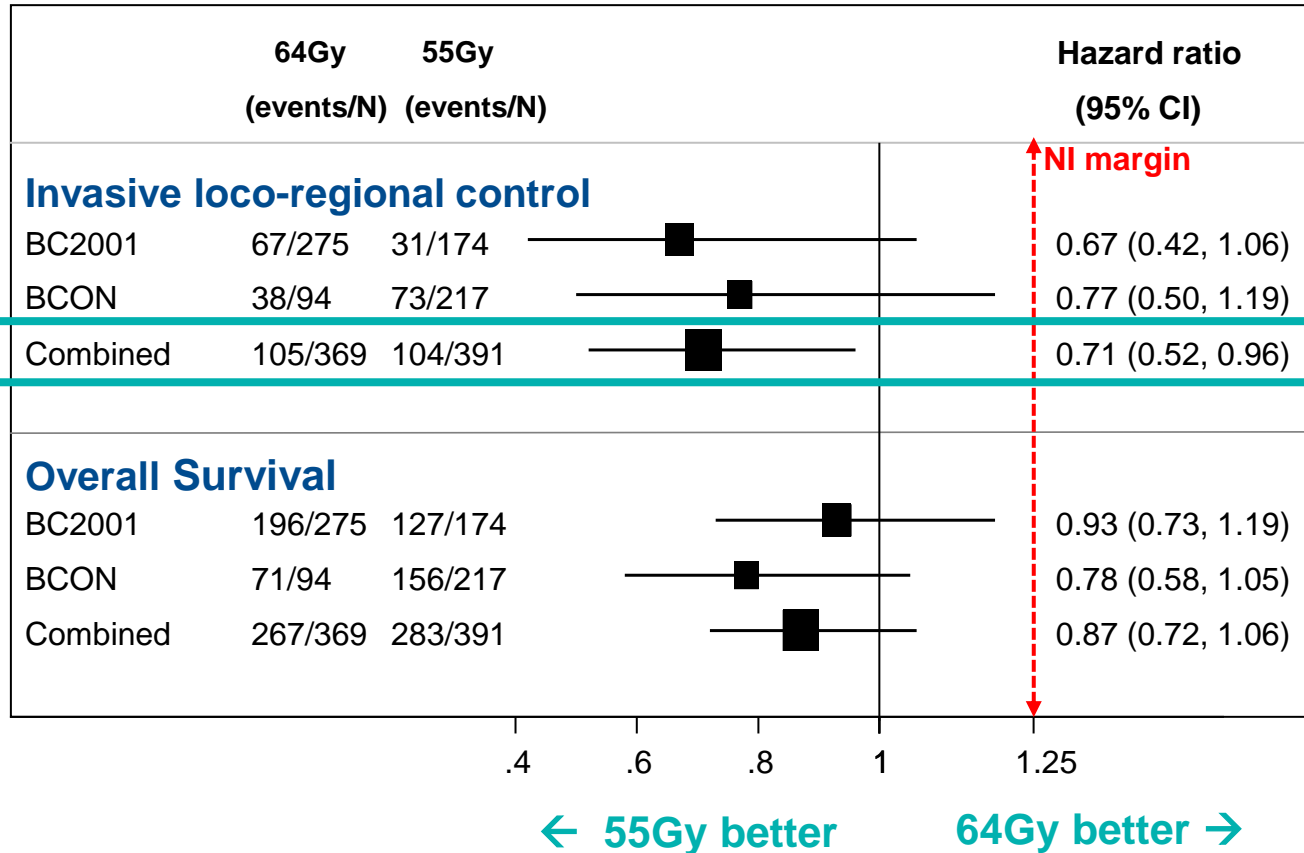
Radiographer led plan selection for bladder IGART



Radiosensitisation is better than radiotherapy alone



55 Gy in 4 weeks is superior to 64 Gy in 6.5 weeks



95% CI excludes non-inferiority margin (p-value < 0.001) AND excludes null difference (superiority p-value 0.026)

55Gy ILRC benefit also seen in patients receiving RT alone: HR 0.72 [CI 0.49-1.05]



Is it time to test radiotherapy again?



The BRAVO trial

- 18 months recruitment
- 27% of those approached consented, but 47/50 were from one network
- Suggests that recruiting to surgery v bladder preservation is hard...again

The BRAVO trial

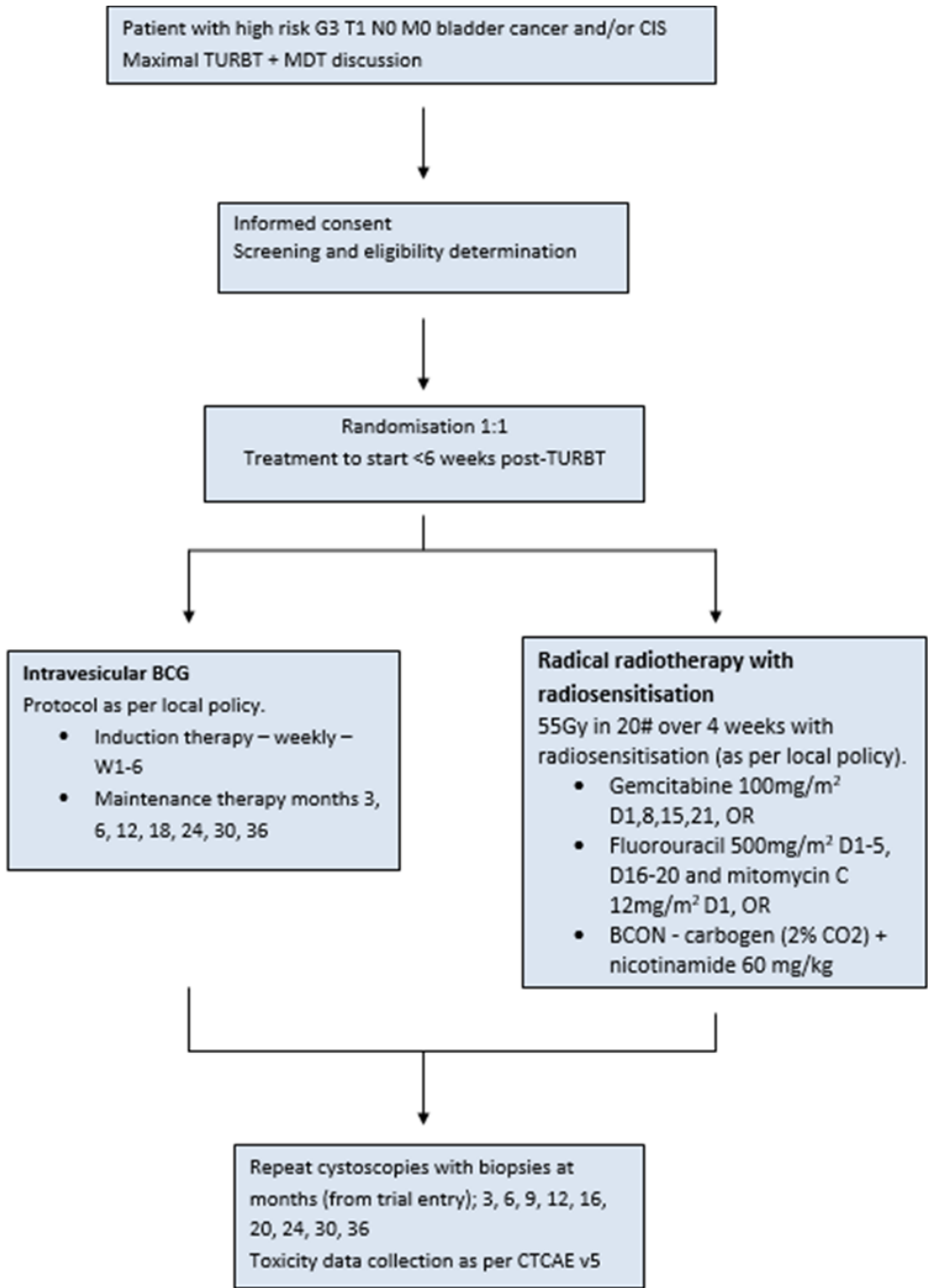
- 18 months recruitment
- 27% of those approached consented, but 70% were from one network
- Suggests that recruitment for surgery v bladder preservation is hard...as

Plenty of phase II data, how do we do the phase III trial?

Trial schema

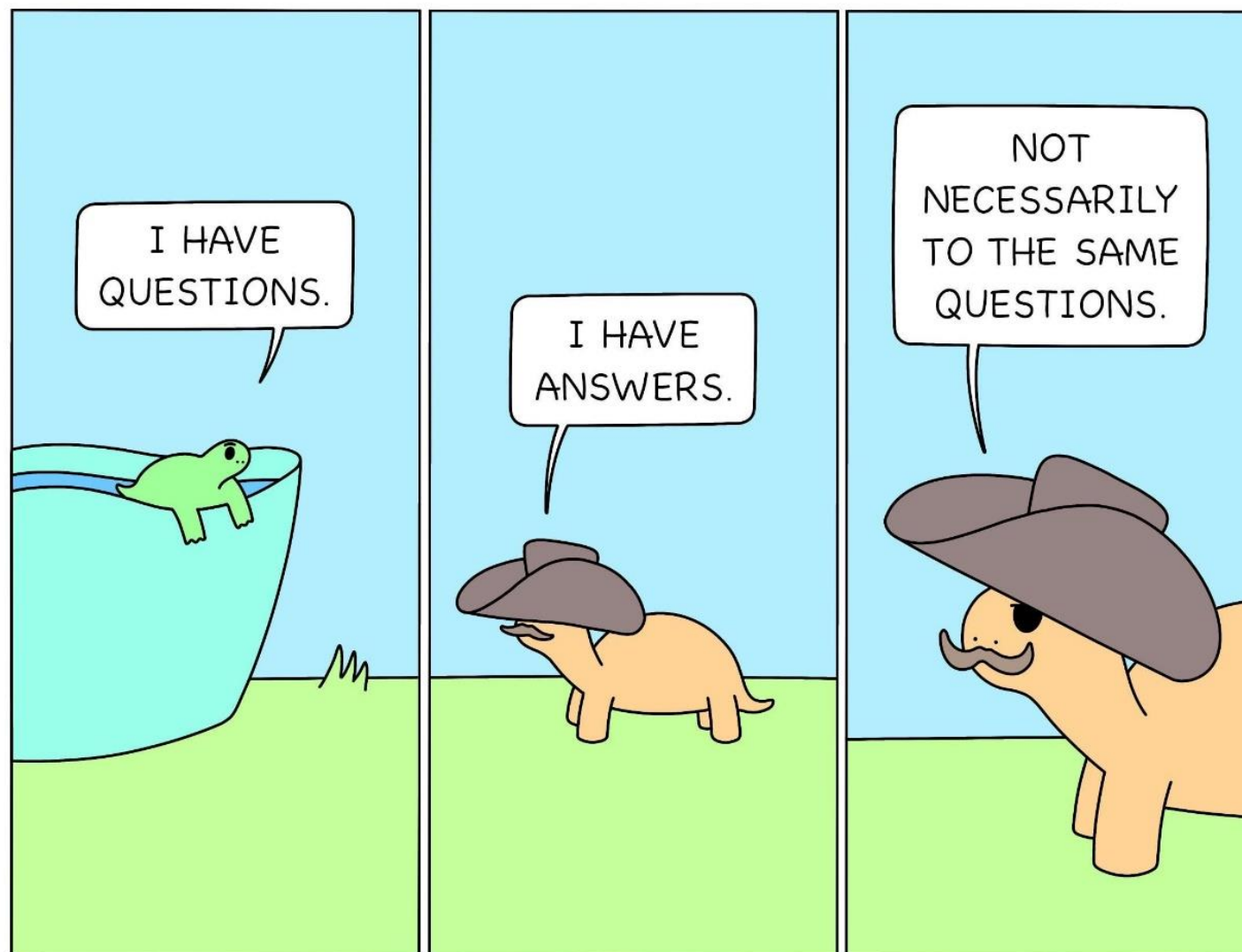
Intravesicular BCG
Protocol as per local policy;

- Induction therapy; weekly for 6 weeks
- Maintenance therapy; months 3, 6, 12, 18, 24, 30, 36



Radical radiotherapy with radiosensitisation
55Gy in 20# over 4 weeks with radiosensitisation (as per local policy);

- Gemcitabine 100mg/m² D1,8,15,21
- Fluorouracil 500mg/m² D1-5, D16-20 and mitomycin C 12mg/m² D1
- BCON - carbogen (2% CO₂) + nicotinamide 60 mg/kg



@workingtheangles



Questions?

