

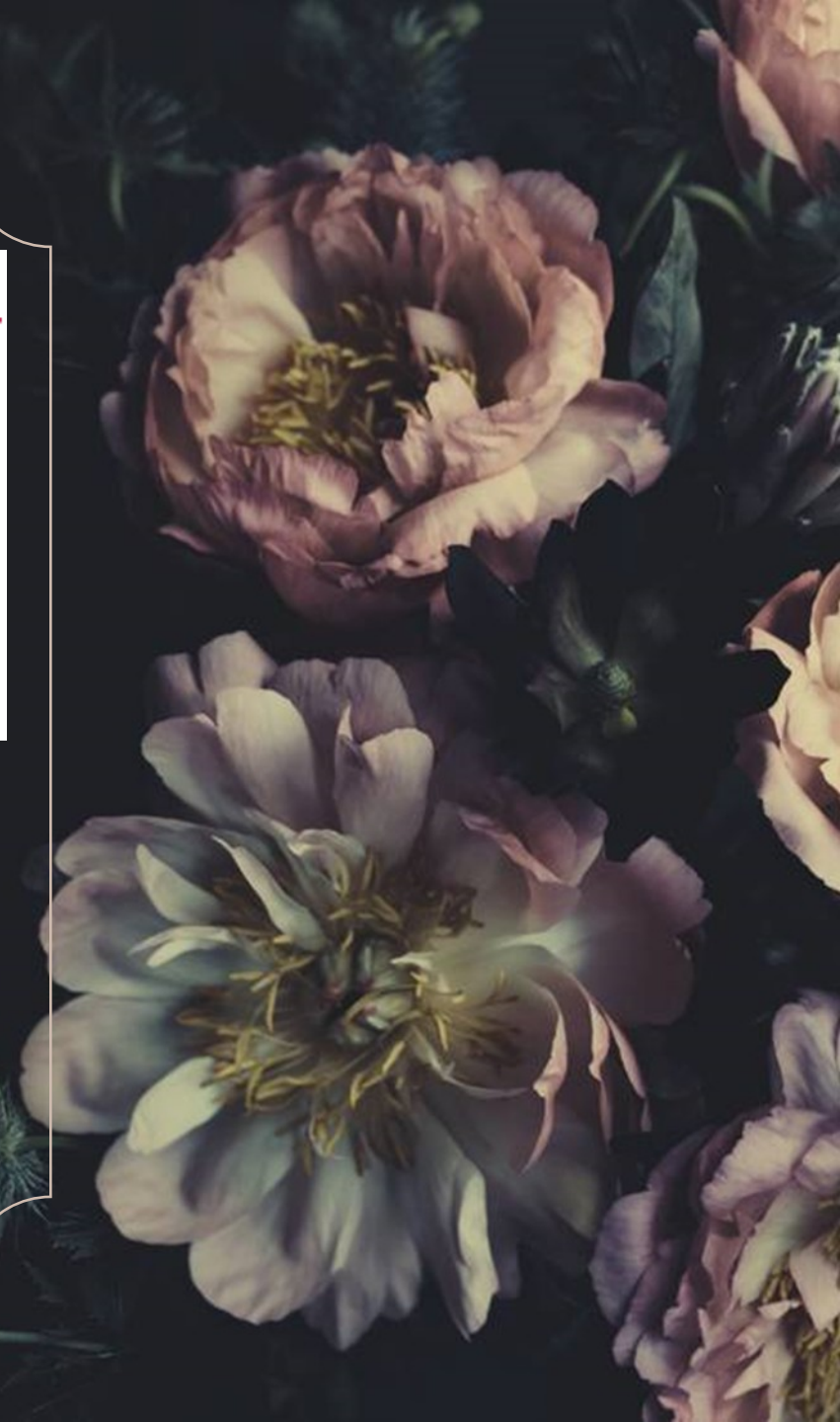


Adjuvant chemotherapy in upper tract urothelial carcinoma (the POUT trial): a phase 3, open-label, randomised controlled trial
















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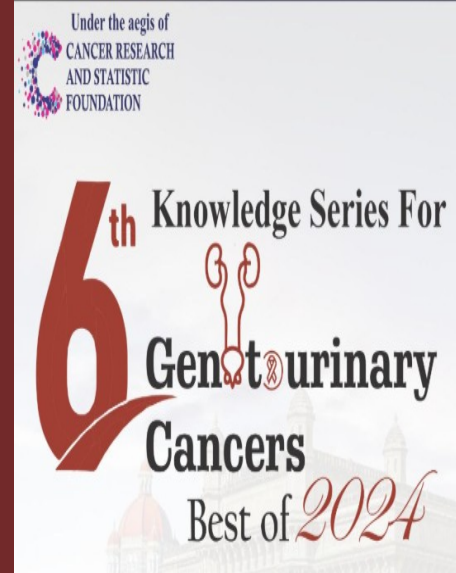
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⑥ Improved Disease-Free Survival With Adjuvant Chemotherapy After Nephroureterectomy for Upper Tract Urothelial Cancer: Final Results of the POUT Trial

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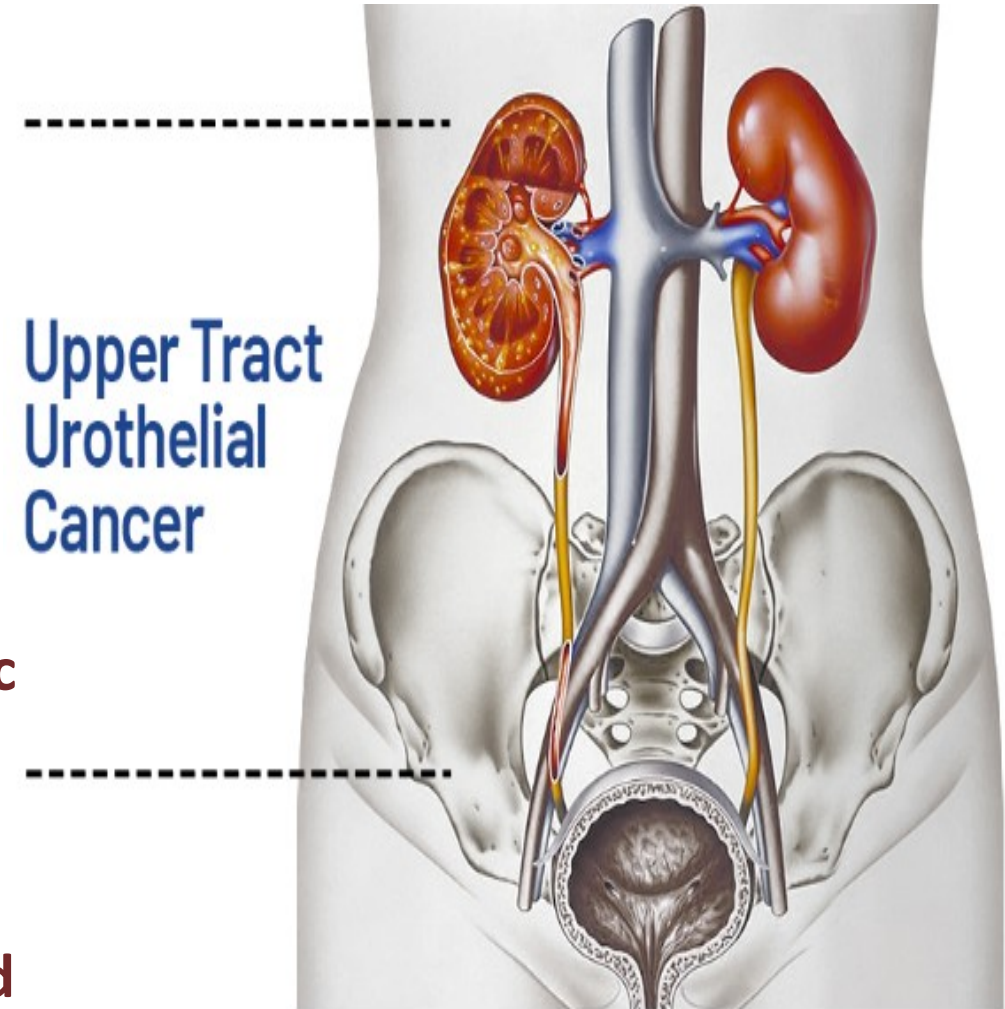
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Peri-Operative chemotherapy versus sUrveillance in upper
Tract urothelial cancer

Background

- **UTUC Rarely occurring tumor : ~5% of all urothelial carcinoma (2-4 cases per 100,000 individuals)**
- **Gold standard treatment → radical nephroureterectomy, via an open or laparoscopic approach.**
- **Patients with muscle invasive UTUC have a high rate of locoregional nodal metastases, associated with poorer outcome.**



Evidence for chemotherapy in UTUC

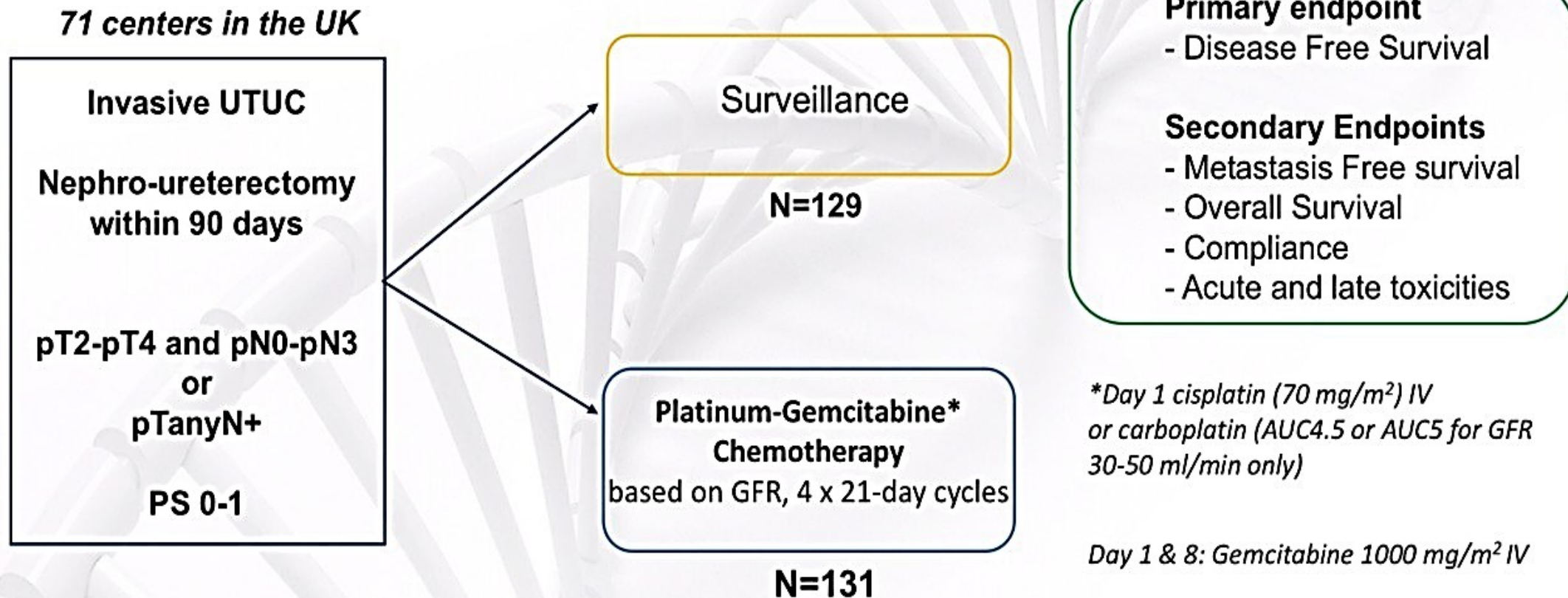
- Small retrospective data: 64 patients were included and no differences in disease-free survival (DFS) or overall survival were seen.
- Another small retrospective review included 43 patients who were offered adjuvant chemotherapy, 32 patients received chemotherapy, the remaining 11 refused.
- All had locally advanced (T3) or node positive disease.
- With 30 months median follow up, DFS was 63.6% vs. 37.5%.

Why not neoadjuvant chemotherapy in UTUC?

- Difficult to obtain definitive histology and accurate staging pre-operatively.
- One study has shown that 12.8% of patients presumed on radiological and clinical grounds to have an UTUC had no tumour subsequently found in the surgical specimen.

Study Design

**Adjuvant chemotherapy in upper tract urothelial carcinoma (the POUT trial):
a phase 3, open-label, randomized controlled trial**



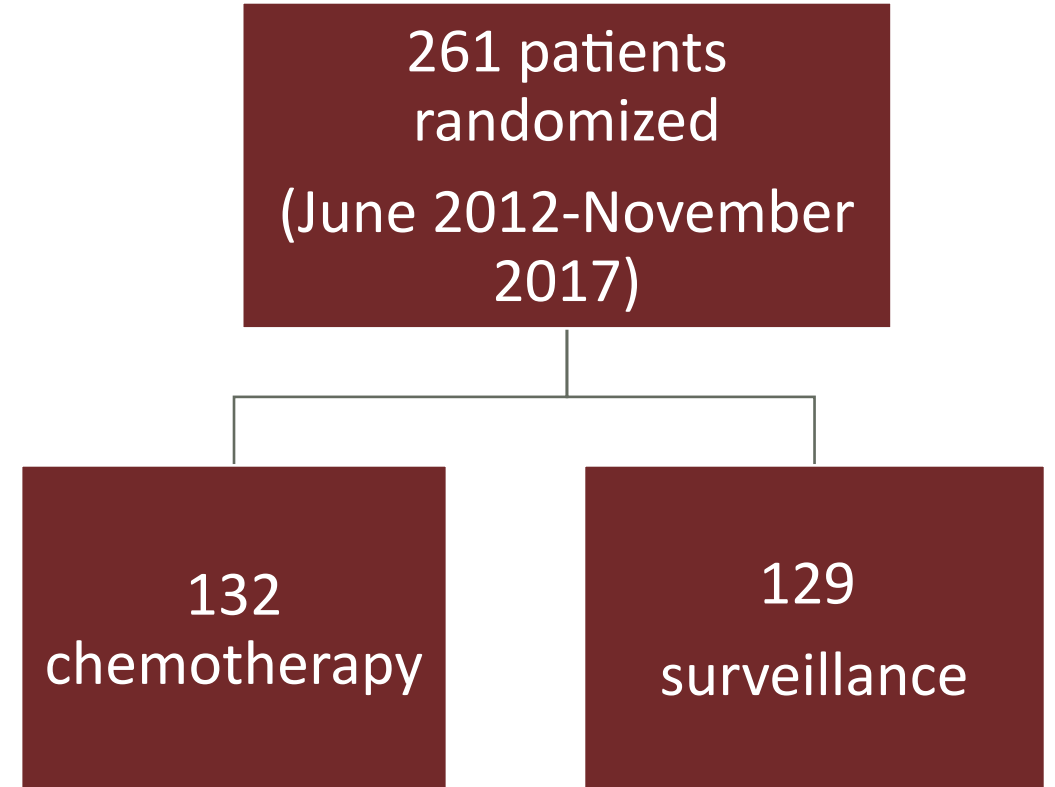
First dedicated randomized phase 3 trial of perioperative chemotherapy for UTUC

Baseline characteristics

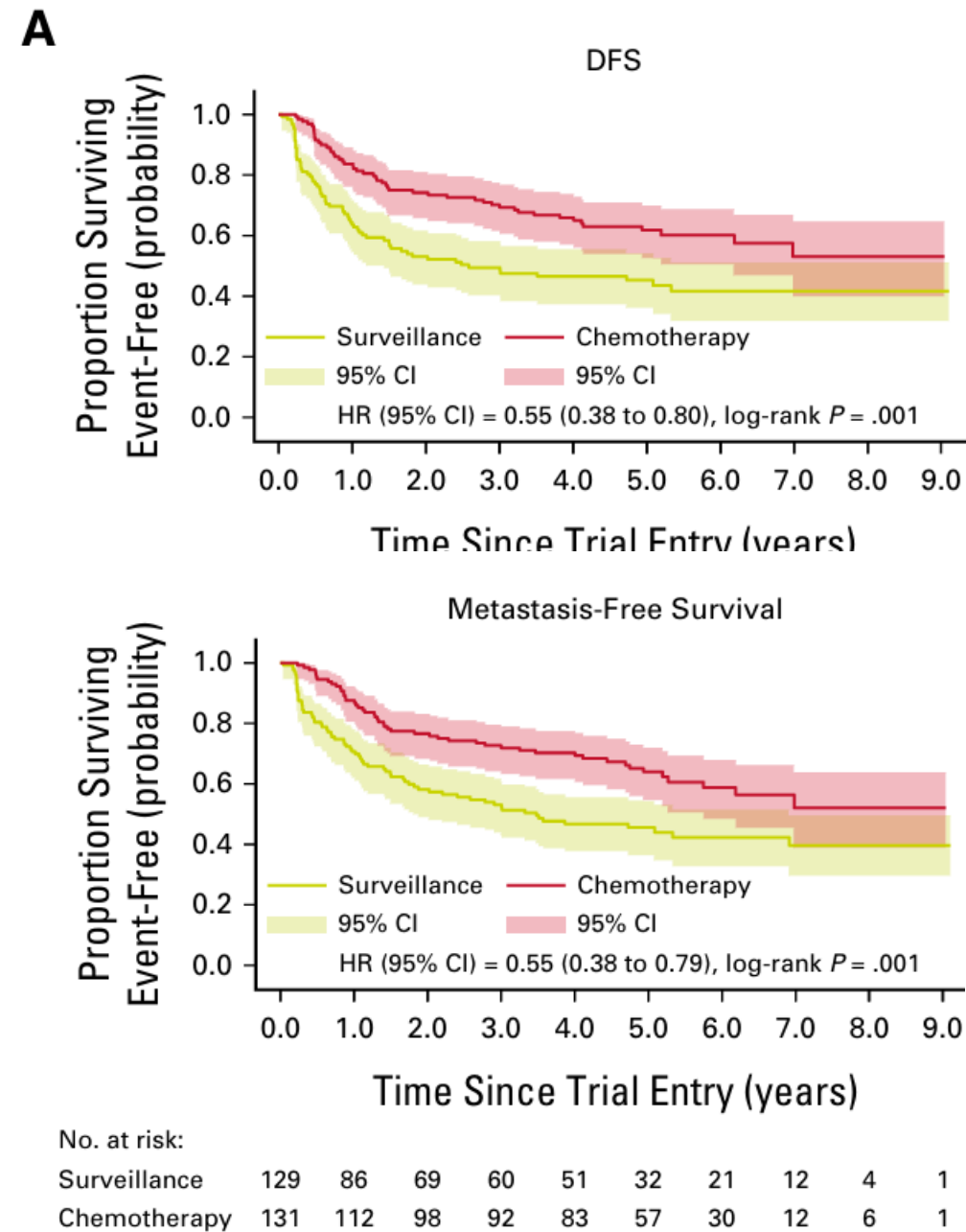
	Surveillance (n=129)	Chemotherapy (n=131)	Total (n=260)
Sex			
Male	83 (64%)	93 (71%)	176 (68%)
Female	46 (36%)	38 (29%)	84 (32%)
Pathological T stage			
pT2	30 (23%)	44 (34%)	74 (28%)
pT3	88 (68%)	83 (63%)	171 (66%)
pT4	11 (9%)	4 (3%)	15 (6%)
Nodal stage*			
N0	118 (91%)	118 (90%)	236 (91%)
N1	7 (5%)	8 (6%)	15 (6%)
N2	4 (3%)	4 (3%)	8 (3%)
N3	0 (0%)	1 (1%)	1 (<1%)
GFR (mL/min)			
30-49	45 (35%)	49 (37%)	94 (36%)
≥50	84 (65%)	82 (63%)	166 (64%)

RESULTS

- Median follow-up was 65 months
- DFS events:
 - chemotherapy arm : 50
 - surveillance groups : 67
- 5-year DFS 62% vs 45% [HR:0.55]

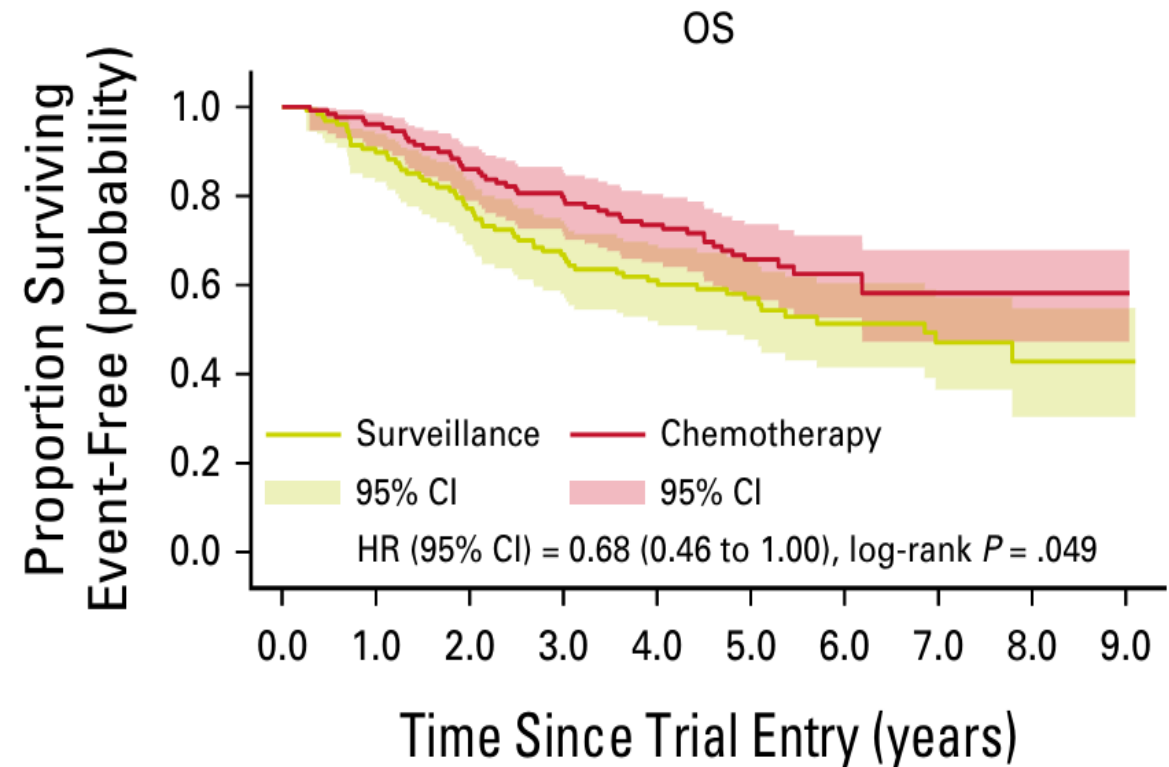


- Non proportional hazards were evident and the RMST for DFS was 72 and 54 months, respectively, an **18-month improvement** in the chemotherapy arm (6 months to 30 months $P=0.003$).
- Metastasis Free Survival and Disease Specific Survival results similarly suggested a benefit of chemotherapy.
- No impact of chemotherapy on TSPB (time to second primary in bladder).



Overall Survival

- Deaths due to urothelial cancer
 - Chemotherapy arm: 46(72%)
 - Surveillance groups: 60(80%)
- 5-year OS 66% v 57%; univariable HR, 0.68, $P=0.049$
- The RMST was 78 and 67months.
- An 11-month OS improvement with chemotherapy (95%CI, 1 to 21 $P=0.036$).

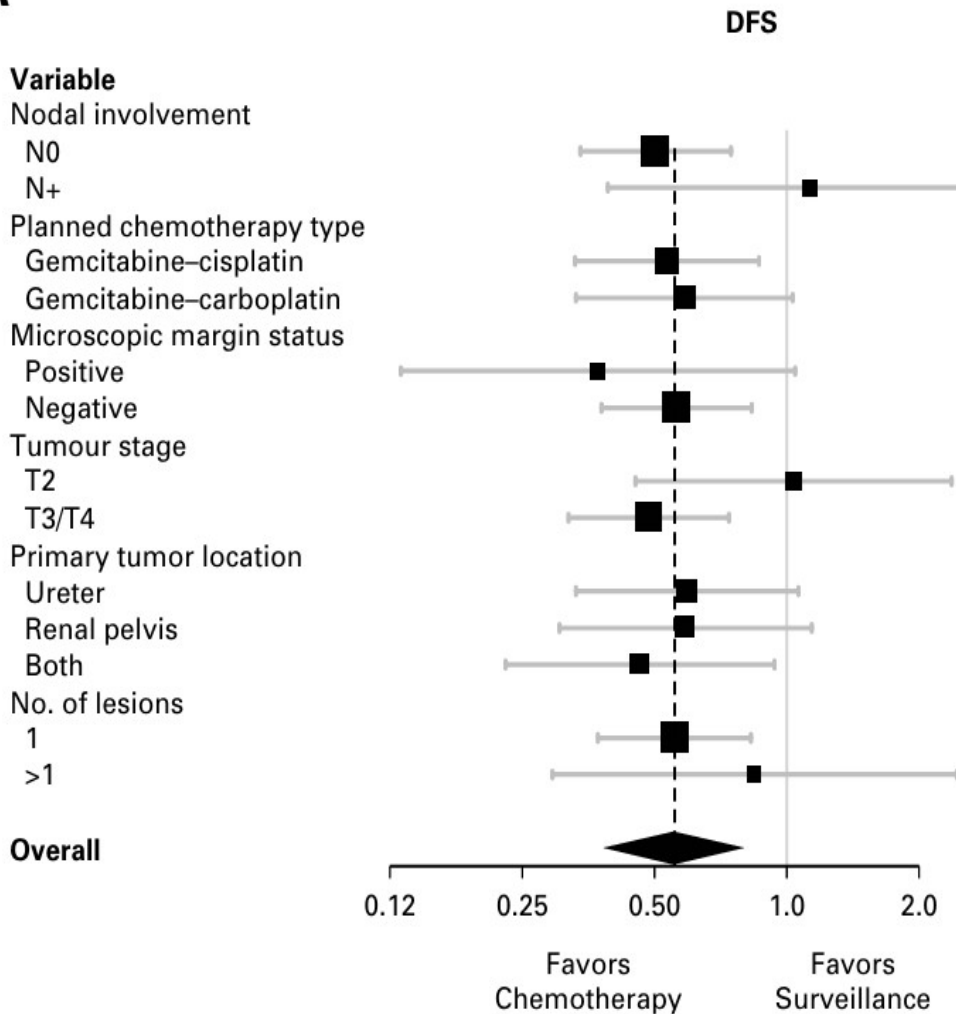


No. at risk:

Surveillance	129	114	97	82	72	46	31	19	7	2
Chemotherapy	131	124	111	103	92	62	35	15	6	1

The treatment effect was consistent across subgroups

A



B

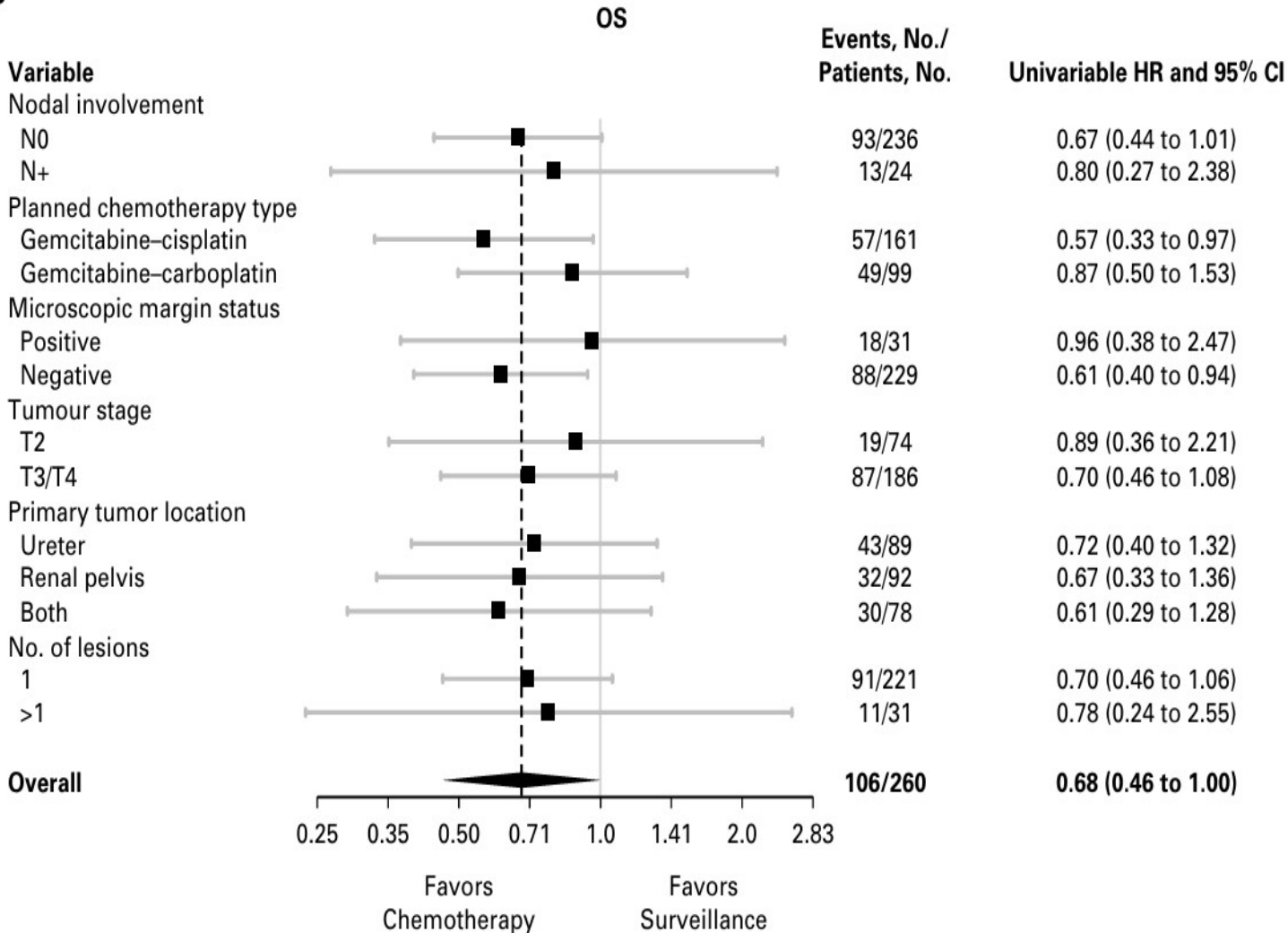


TABLE A3. Late Toxicity Reported Between 6 and 24 Months Postrandomization (censored within 3 months of progression)

Follow-Up Time (postrandomization)	Maximum CTCAE Grade Reported	Surveillance, No. (%)	Chemotherapy, No. (%)	Total, No. (%)
Month 12 (n=222)	Grade <3	90 (87.4)	107 (89.9)	197 (88.7)
Surveillance (n=103)	Grade 3-5	7 (6.8)	10 (8.4)	17 (7.7)
Chemotherapy (n=119)				
Month 18 (n=198)	Grade <3	79 (86.8)	97 (90.7)	176 (88.9)
Surveillance (n=91)	Grade 3-4	6 (6.6)	9 (8.4)	15 (7.6)
Chemotherapy (n=107)				
Month 24 (n=177)	Grade <3	77 (92.8)	85 (90.4)	162 (91.5)
Surveillance (n=83)	Grade 3-4	6 (7.2)	9 (9.6)	15 (8.5)
Chemotherapy (n=94)				
Maximum overall (n=240)	Grade <3	95 (81.2)	98 (79.7)	193 (80.4)
Surveillance (n=117)	Grade 3-5	22 (18.8)	25 (20.3)	47 (19.6)
Chemotherapy (n=123)				

DISCUSSION

- Primary results from POUT have already changed practice on the basis of the DFS benefit.
- A statistically significant OS benefit of 11 months over a 9-year period, with the peak benefit between 3 and 4 years.
- Combined with improvements in Metastasis Free Survival and Disease Specific Survival, these results add weight to the sustained DFS benefit.

- The POUT primary analysis showed acceptable levels of acute toxicity with chemotherapy, in line with previous reports.
- The current data suggests no important long-term adverse impacts, which might offset the benefits.
- Systemic therapy on relapse was less frequent in those who received adjuvant chemotherapy than those in the surveillance group.
- While chemotherapy reduces time to metastasis, it appeared to have no impact on the evolution of second primary formation in the bladder.
- **In summary, updated outcomes from the POUT trial add further support to the value of adjuvant systemic gemcitabine+platinum combination chemotherapy after nephroureterectomy for UTUC**

Thank you

