

# **Discussion Abstracts**

## **7860, 7870 and 7880**

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# **No disclosures**

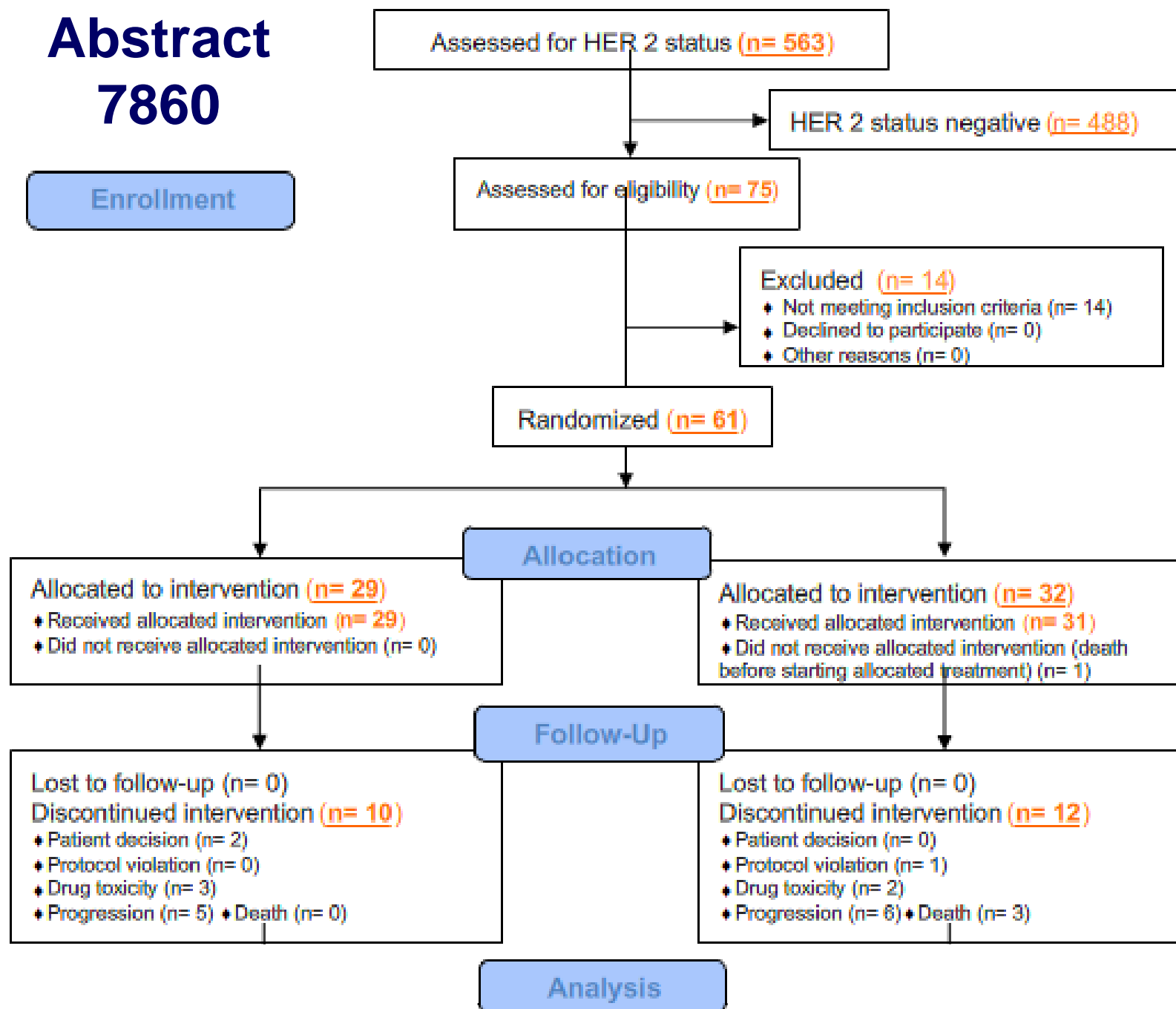
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# Discussion Abstract 7860

## **Multicenter randomized phase 2 trial of Gemcitabine - Platinum with or without Trastuzumab in advanced or metastatic urothelial carcinoma with HER2 overexpression**

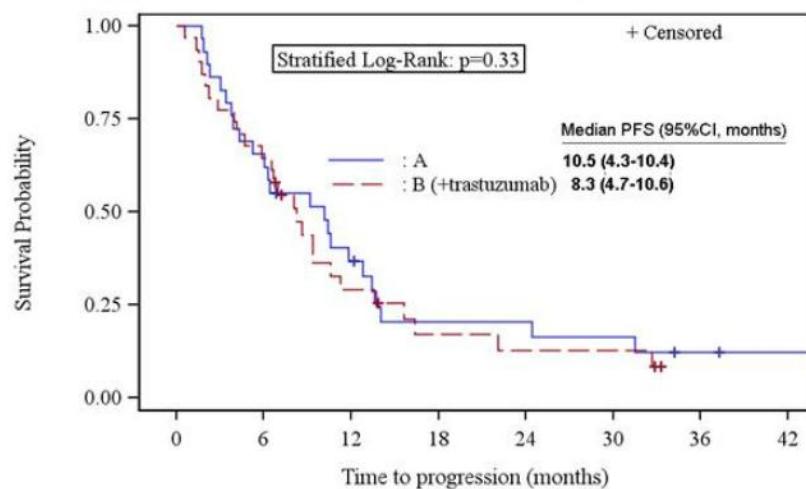
Stéphane Oudard<sup>1</sup>, Stéphane Culine<sup>2</sup>, Annick Vieillefond<sup>3</sup>, Franck Priou<sup>4</sup>, François Goldwasser<sup>3</sup>, Alain Ravaud<sup>5</sup>, Gwenaëlle Gravis<sup>6</sup>, Gael Deplanque<sup>7</sup>, Jean-Pascal Machiels<sup>8</sup>, Eric Voog<sup>9</sup>, Jean Michel Vannetzel<sup>10</sup>, Jean Louis Misset<sup>11</sup>, Laurent Mignot<sup>12</sup>, Christine Theodore<sup>12</sup>, Xavier Muracciole<sup>13</sup>, Jacques Olivier Bay<sup>14</sup>, Xavier Pivot<sup>15</sup>, Philippe Beuzeboc<sup>16</sup>

# Abstract 7860



# Abstract 7860

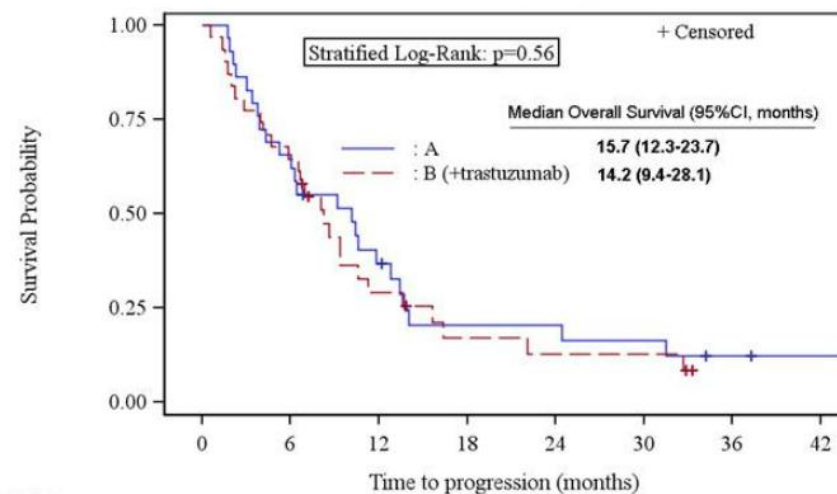
## Progression-Free Survival (PFS)



At risk:

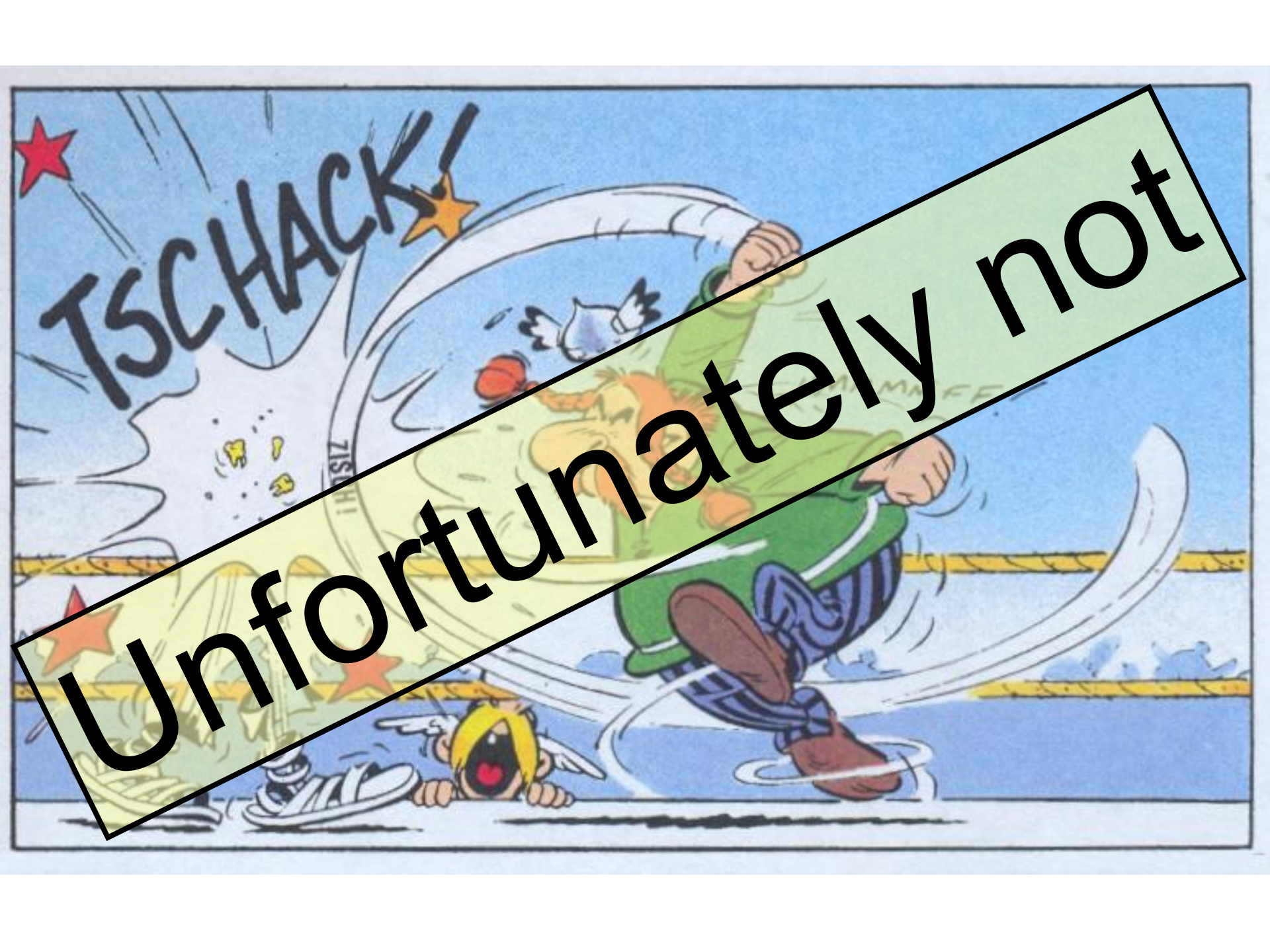
A	29	19	10	5	3	4	2	1
B (+trastuzumab)	31	20	8	4	3	4	0	1

## Overall Survival (OS)



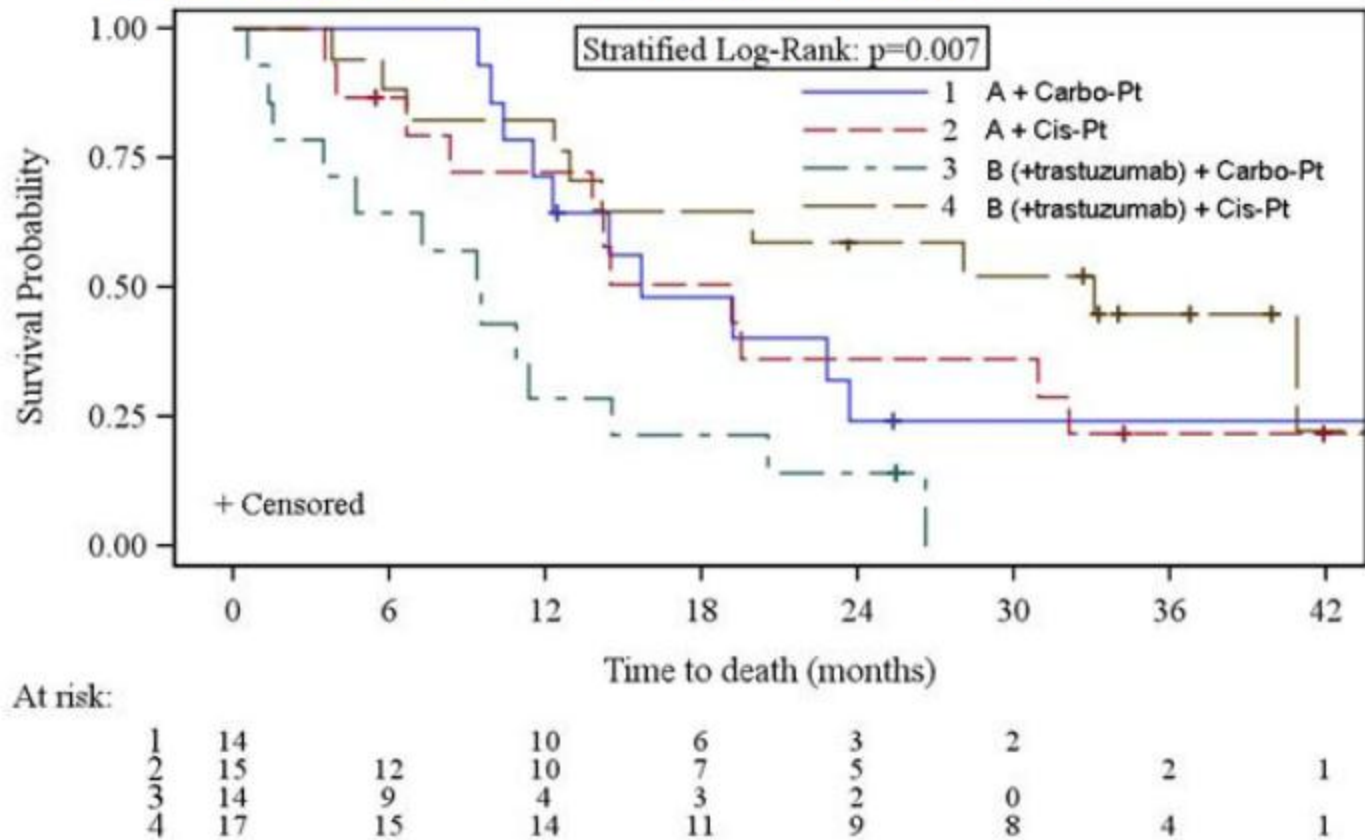
At risk:

A	29	19	10	5	3	4	2	1
B (+trastuzumab)	31	20	8	4	3	4	0	1



Abstract  
7860

Descriptive Results:  
OS related to baseline platinum



Median OS

	-	+
	15.7 (12.3 – 22.8)	14.2 (9.5 – 28.1)
cisplatin based-CT	14.5 (6.7 – 30.9)	33.1 (12.4 – 50.0)
carboplatin based-CT	15.7 (10.4 – 23.7)	9.4 (1.5 – 14.6)

## Abstract 7860

### Conclusions

- HER2 over-expression is rare in advanced and/or mUCs
  - No difference on ORR, PFS, OS and Quality of Life between CG +/- trastuzumab was observed
  - CG-trastuzumab was feasible –(with more febrile neutropenia, LVEF decreased and dyspnea)
  - Baseline serum HER2 level was predictive of PFS whatever the treatment
- Trastuzumab could have a synergetic effect with cisplatinum drug leading to a longer OS



# Discussion Abstract 7870

**External validation of the association of progression-free survival at 6 months (PFS6) with overall survival at 12 months (OS12) in second-line therapy for advanced urothelial carcinoma (UC)**

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# Abstract

## 7870

## Methods

- Progression was defined as objective tumor progression or death.
- In the discovery dataset, 10 phase II trials (N=689) evaluating second-line therapy after perioperative chemotherapy only or chemotherapy for metastatic disease were combined with individual patient level data.
- The relationship between PFS6/RR and OS12 was assessed at the trial level using Pearson correlation and weighted linear regression.
- The relationship between PFS6/response and OS12 at the individual level was assessed using Pearson chi-square test with Yates continuity correction.
- External validation was conducted in a second-line phase III trial, N=370 (Bellmunt J et al, JCO 2009).

# Abstract

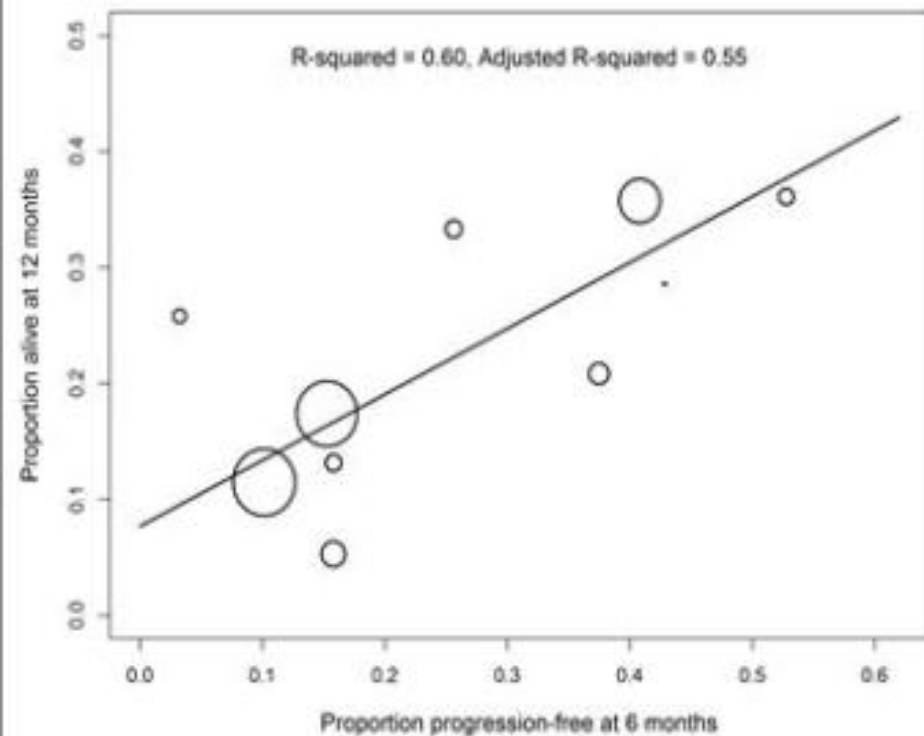
## 7870

## Methods

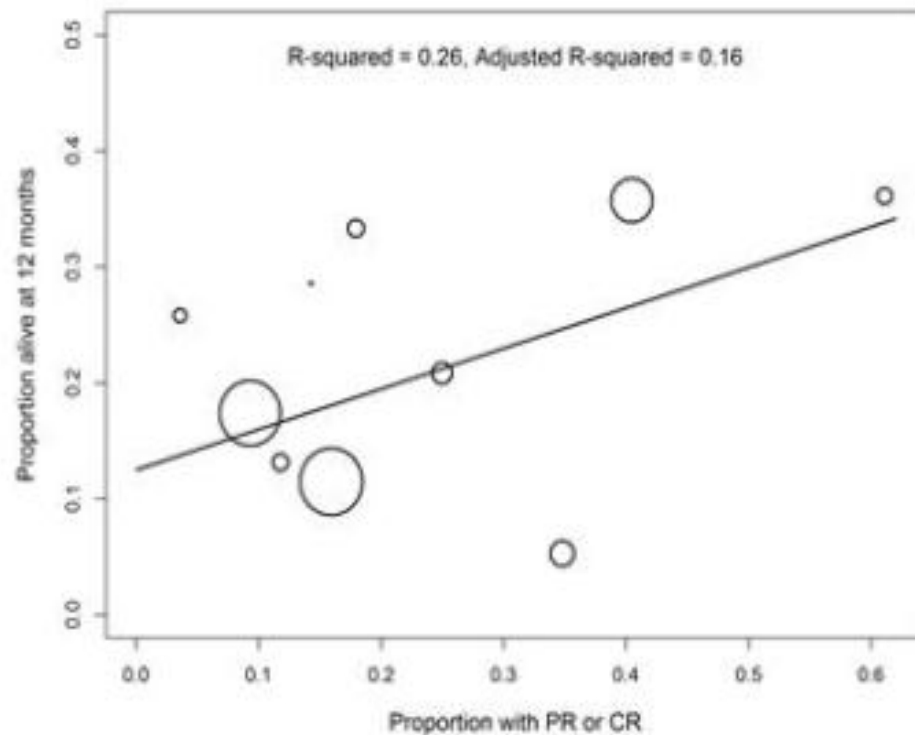
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# Abstract 7870

Trial level relation between PFS6 and OS12



Trial level relation between OS12 and RECIST response



# Abstract

## 7870

### Conclusion

- PFS6 is robustly associated with OS12 at the trial and individual patient levels in second-line therapy for advanced UC receiving chemotherapy and/or biologic agents.
- Response was not statistically associated with OS12 at the trial level and displayed a weaker association at the individual level.
- PFS6 may be a more optimal endpoint to capture the durable benefits of agents being screened in phase II trials
- The magnitude of improvement in PFS6 that translates to extension of OS is unclear: improvement in PFS6 from 13.25% with BSC to 26.48% with vinflunine plus BSC translated to 23% reduction in hazard of death.

# Progression-Free Survival: Meaningful or Simply Measurable?

## Advantages & Disadvantages of PFS

- *(relatively)* easy to measure
- early event in most tumors
- may indicate activity of a new agent
- may correlate *(somewhat)* with overall survival
- however it is **not** a measure of patient benefit

useful endpoint of phase II trial

# The Price We Pay for Progress: A Meta-Analysis of Harms of Newly Approved Anticancer Drugs

*Saroj Niraula, Bostjan Seruga, Alberto Ocana, Tiffany Shao, Robyn Goldstein, Ian F. Tannock, and Eitan Amir*

New anticancer agents that lead to improvements in time-to-event end points also increase morbidity and treatment-related mortality.

# Discussion Abstract 7880

**Neoadjuvant (NACT) and Adjuvant Chemotherapy  
(ACT) for Muscle-Invasive Bladder Cancer (MIBC):**

**A Population-Based Outcomes Study in Ontario Canada**

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**Cancer Care Ontario Chair in Health Services Research**

**Division of Cancer Care and Epidemiology**

**Queen's University, Kingston, Canada**



The Cancer Research Institute at Queen's University  
Division of Cancer Care and Epidemiology

# Bladder Cancer - who will survive ?

AJCC Stage (5th Edition)	Cases	Percent	Median Survival Time (Months)	5-Year Relative Survival Rate (%)		
				Obs	Exp	Rel
Total	67,528	100.0	101.1	63.7	77.8	81.9
Stage 0	29,638	43.9	> 120	78.0	79.3	98.4
Stage I	8,611	12.8	108.3	68.1	77.7	87.7
Stage II	4,541	6.7	54.6	47.7	76.2	62.6
Stage III	2,496	3.7	28.3	35.8	78.7	45.5
Stage IV	3,775	5.6	9.7	11.8	79.9	14.8
Unknown	18,467	27.3	80.6	57.4	75.3	76.3

# Study Design

- Population-based, retrospective cohort study to describe management and outcome of all cases of resected MIBC in the Canadian province of Ontario 1994-2008.



# Methods (2)

- Electronic records of treatment were linked to the OCR to describe use of surgery, RT and chemotherapy.
- The OCR does not have detailed stage information. Accordingly, surgical pathology reports were obtained to assign pathologic T and N stage.
- For the NACT/ACT analyses we included only those cases with muscle-invasive TCC.
- Survival analyses performed using Cox model and propensity score techniques.

**Abstract  
7880**



# Results: Study Cohort

- Among 4876 cystectomy cases pathology reports have thus far been obtained for 3429 (70%)

➡ 2738 cases with muscle-invasive TCC

- Characteristics of 2738 MIBC cases

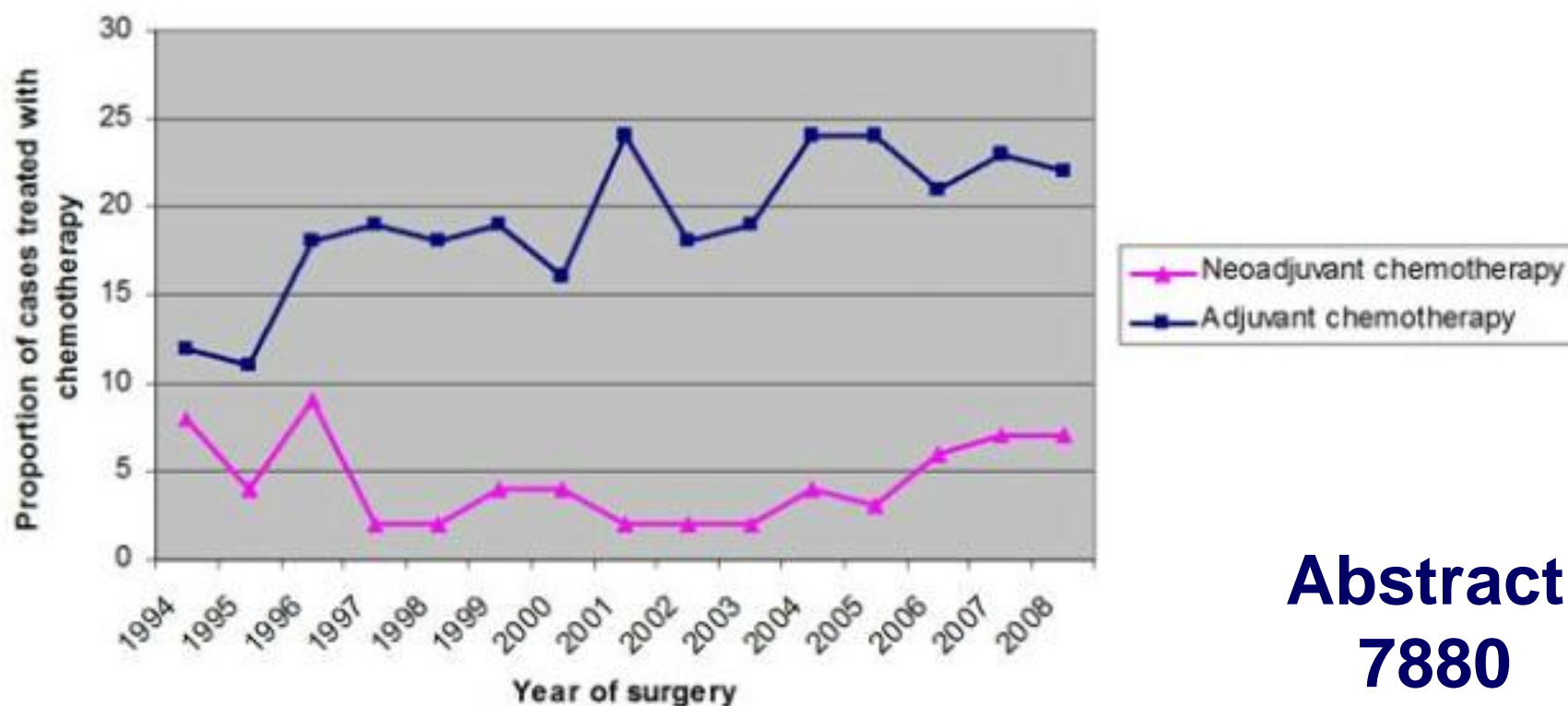
Age, years	
20-49	95 (3%)
50-59	335 (12%)
60-69	681 (25%)
70-79	1095 (40%)
80+	532 (19%)
Sex	
Male	2061 (75%)
Female	677 (25%)
T stage	
<T3	807 (29%)
T3-T4	1931 (71%)
N stage	
N negative	1195 (44%)
N positive	702 (26%)
NX	841 (31%)

**Abstract  
7880**

# Results: NACT/ACT Utilization

- Utilization of NACT was fairly stable over time (4%)
- Utilization of ACT increased over time

➡ 16% (94-98), 19% (99-03), 23% (04-08),  $p=0.001$



**Abstract  
7880**



I can't see anything !

It's so small

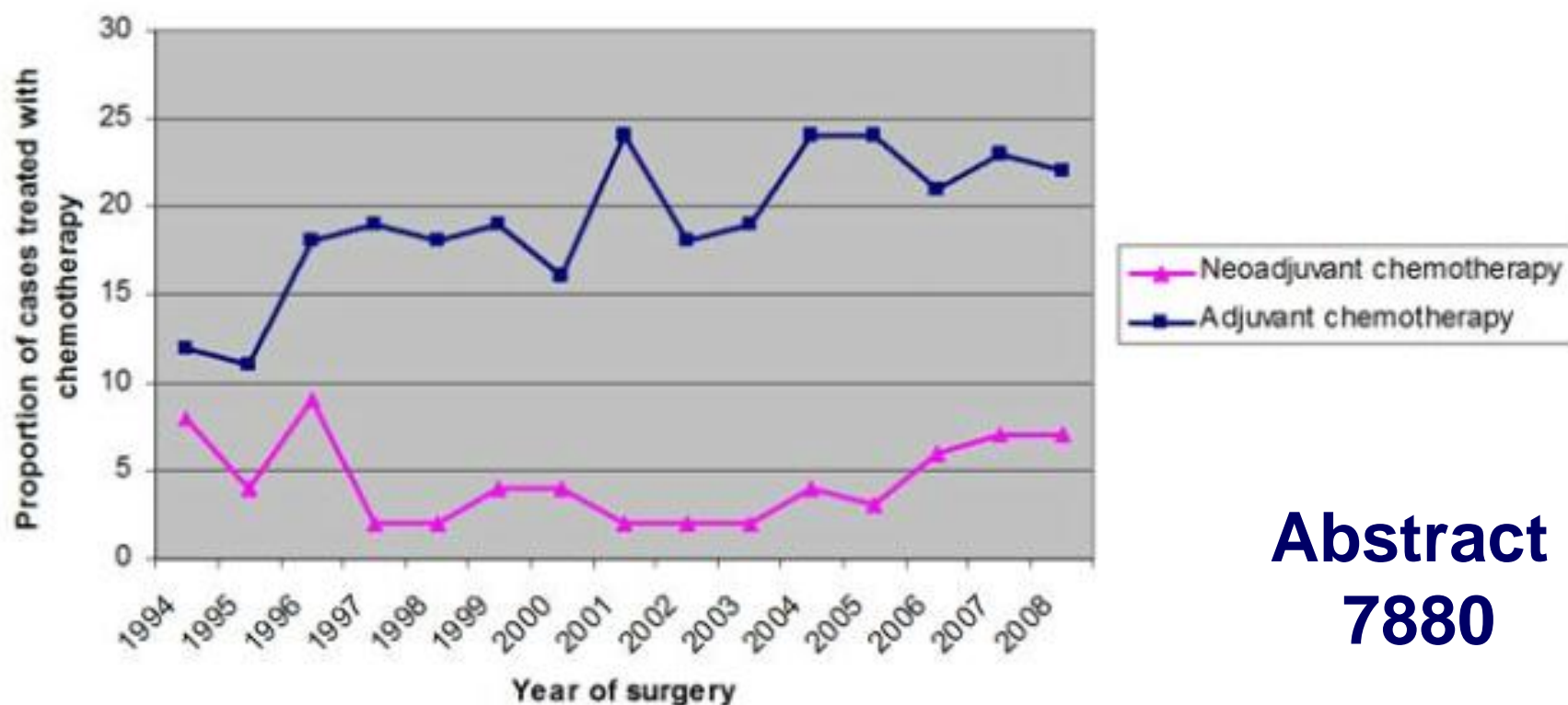
Nay, it's at least that big

Has this any relevance at all ?

# Results: NACT/ACT Utilization

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**Abstract  
7880**

➔ are physicians following guidelines?

➡ are physicians following guidelines?

**Well quite obviously they do not,  
but what else impacts on their behavior?**

