

HOPITAL UNIVERSITAIRES PARIS NORD VAL DE SEINE

Université de Paris

## Management of favorable outcomes after neoadjuvant chemotherapy



**you** Young Academic Urologists

**EAU** European Association of Urology

**Evangoulos Xylina, MD, PhD, FFBU**  
Associate Professor of Urology  
Bichat-Claude Bernard Hospital  
Paris University, France

## Conflict of Interest

- Advisory Board: Ipsen Pharma, Janssen, Ferring, Astrazeneca.
- Invited speaker: Ipsen Pharma, Janssen.
- Principal investigator: Roche, Merck, Astrazeneca, Ferring, Janssen, Pfizer.
- Board Member of the French Health Technology Assessment Agency (Haute Autorité de Santé).

## Outline

- ✓ Neoadjuvant chemotherapy is the standard of care.
- ✓ No residual disease = surrogate of overall survival.
- ✓ Outcomes of patients with no residual disease after TURB and neoadjuvant chemotherapy without local treatment.
- ✓ Ongoing trials and future.

## Outline


- ✓ **Neoadjuvant chemotherapy is the standard of care.**
- ✓ No residual disease = surrogate of overall survival.
- ✓ Outcomes of patients with no residual disease after TURB and neoadjuvant chemotherapy without local treatment.
- ✓ Ongoing trials and future.

## Current Guidelines

### EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer

Recommendations	Strength rating
Offer neoadjuvant chemotherapy (NAC) for T2-T4a, cN0M0 bladder cancer. In this case, always use cisplatin-based combination therapy.	Strong
Do not offer NAC to patients who are ineligible for cisplatin-based combination chemotherapy.	Strong

J.A. Witjes (Chair), M. Bruins, R. Cathomas, E. Comperat, N.C. Cowan, G. Gakis, V. Hernández, A. Lorch, M.J. Ribal (Vice-chair), G.N. Thalmann, A.G. van der Heijden, E. Veskimäe



## Current Guidelines

+

- Tolerability of chemotherapy and patient compliance > in pre-cystectomy setting.
- Patients might respond to NAC and reveal a favourable pathological status, determined mainly by achieving pT0, pN0 and help negative surgical margins status.
- Neoadjuvant chemotherapy does not seem to affect the outcome of surgical morbidity.

-

- Delayed cystectomy might compromise the outcome in patients not sensitive to chemotherapy, (# negative effect of delayed cystectomy only include chemo-naïve patients).
- Clinical staging using bimanual palpation, CT or MRI may result in over- and understaging and have a staging accuracy of only 70% leading to overtreatment.

=

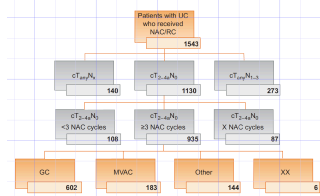
- Neoadjuvant chemotherapy should only be used in patients eligible for cisplatin combination chemotherapy; other combinations (or monotherapies) are inferior.

## Current Guidelines

### Multicenter Assessment of Neoadjuvant Chemotherapy for Muscle-invasive Bladder Cancer

#### METHODS

- ✓ NAC Consortium
- ✓ 18 centers
- ✓ 1130 cT2-4N0 patients
- ✓ 935 at least 3 NAC cycles



Herrington Ziegler\*, Patrick N. Eggen\*, Adrian S. Poincy\*, Laura S. Merritt\*,  
 Colin P. Dwyer\*, Maria C. Alar\*, Lorenz-Maria Kreibitz\*, Mikko S. Koskela\*,  
 Peter V. Van\*, David Vignaud\*, Francesco Vignaud\*, Nicholas J. Compton\*, William Kattan\*,  
 Alan A. Chalfant\*, Joelle S. Gagnon\*, Christel E. Gagnon\*, James Cunningham\*,  
 John A. McCreedy\*, Jonathan Anagnostou\*, Shabbir F. Shariat\*, Jonathan E. Wright\*,  
 Andrew C. Thompson\*, Todd M. Morgan\*, Jeff M. Hollender\*, Timothy J. Brannan\*,  
 John H. Kim\*, Michael A. Brennan\*, Paul Gnanapavan\*, Joseph A. Sparano\*,  
 Jay B. Shah\*, Alex W. van Rhijn\*, Steffen Ditschuneck\*, Philipp E. Spiess\*, Peter C. Black\*

## Current Guidelines

### Multicenter Assessment of Neoadjuvant Chemotherapy for Muscle-invasive Bladder Cancer

#### RESULTS

	pT0 (pCR)	pTis/pT1 (pR)	pT1N0 (pR)	pT2N0	pT3-4N0	pTany N1-3	pTis or N2	Total
MIVAC NAC, n (%)	21 (23.0)	44 (48.3)	13 (14.0)	12 (13.0)	19 (21.0)	3 (3.3)	91	
CT	16 (29.6)	8 (14.8)	24 (44.6)	11 (20.4)	10 (18.5)	0 (0.0)	54	
CTx	5 (15.6)	7 (21.8)	12 (37.5)	2 (6.2)	9 (27.8)	0 (0.0)	32	
CTx	1 (3.0)	2 (6.3)	1 (3.0)	1 (3.0)	2 (6.0)	0 (0.0)	6	
Total	40 (24.5)	37 (23.2)	82 (44.8)	27 (14.7)	30 (16.4)	4 (2.3)	183	
GC NAC, n (%)	114 (27.3)	84 (20.0)	198 (47.4)	65 (15.5)	71 (17.0)	10 (2.4)	418	
CT	22 (15.4)	30 (21.0)	52 (36.4)	21 (14.7)	29 (20.3)	1 (0.7)	143	
CTx	8 (15.4)	11 (20.2)	4 (10.2)	14 (25.9)	10 (18.5)	0 (0.0)	39	
CTx	2 (10.0)	2 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2	
Total	144 (23.9)	119 (19.7)	203 (43.7)	90 (15.0)	124 (20.6)	11 (1.8)	602	
Other NAC, n (%)	1 (12.8)	11 (11.7)	25 (24.3)	18 (18.1)	31 (31.0)	3 (3.0)	94	
CT	1 (9.3)	7 (6.2)	5 (15.6)	4 (11.5)	10 (31.2)	1 (3.4)	32	
CTx	7 (38.9)	1 (5.6)	8 (44.4)	1 (5.6)	7 (38.9)	2 (11.3)	18	
CTx	-	-	-	-	-	-	-	
Total	22 (15.3)	14 (9.7)	36 (25)	26 (18)	35 (24.3)	4 (3.0)	144	

Herrington Ziegler\*, Patrick N. Eggen\*, Adrian S. Poincy\*, Laura S. Merritt\*,  
 Colin P. Dwyer\*, Maria C. Alar\*, Lorenz-Maria Kreibitz\*, Mikko S. Koskela\*,  
 Peter V. Van\*, David Vignaud\*, Francesco Vignaud\*, Nicholas J. Compton\*, William Kattan\*,  
 Alan A. Chalfant\*, Joelle S. Gagnon\*, Christel E. Gagnon\*, James Cunningham\*,  
 John A. McCreedy\*, Jonathan Anagnostou\*, Shabbir F. Shariat\*, Jonathan E. Wright\*,  
 Andrew C. Thompson\*, Todd M. Morgan\*, Jeff M. Hollender\*, Timothy J. Brannan\*,  
 John H. Kim\*, Michael A. Brennan\*, Paul Gnanapavan\*, Joseph A. Sparano\*,  
 Jay B. Shah\*, Alex W. van Rhijn\*, Steffen Ditschuneck\*, Philipp E. Spiess\*, Peter C. Black\*

## Current Guidelines

### Multicenter Assessment of Neoadjuvant Chemotherapy for Muscle-invasive Bladder Cancer

#### RESULTS

Study	Year	Study design	Patients treated with CC, n (%)	Patient characteristics	pCR	pPR
Dash et al [15]	2008	Retrospective	42 vs 54	cT2-4N0M0	CC 20%	CC 30%
Kaneko et al [24]	2011	Retrospective	22 vs 9	cT2-4N0-1M0	MIVAC 28%	MIVAC 35%
Yoshida et al [17]	2012	Retrospective	16 vs 45	cT2-4N0-2M0	MIVAC 22%	MIVAC 44%
Pai et al [16]	2012	Retrospective	24 vs 22 vs 15	cT2-4N0M0	CC 25%	CC 50%
Falvey et al [14]	2013	Retrospective	58 vs 58	cT2-4N0M0	MIVAC 22.5%	MIVAC 58%
Mojer et al [25]	2013	Retrospective series	125	cT2-4N0-2M0	CC 21%	CC 33%

Herrington Ziegler\*, Patrick N. Eggen\*, Adrian S. Poincy\*, Laura S. Merritt\*,  
 Colin P. Dwyer\*, Maria C. Alar\*, Lorenz-Maria Kreibitz\*, Mikko S. Koskela\*,  
 Peter V. Van\*, David Vignaud\*, Francesco Vignaud\*, Nicholas J. Compton\*, William Kattan\*,  
 Alan A. Chalfant\*, Joelle S. Gagnon\*, Christel E. Gagnon\*, James Cunningham\*,  
 John A. McCreedy\*, Jonathan Anagnostou\*, Shabbir F. Shariat\*, Jonathan E. Wright\*,  
 Andrew C. Thompson\*, Todd M. Morgan\*, Jeff M. Hollender\*, Timothy J. Brannan\*,  
 John H. Kim\*, Michael A. Brennan\*, Paul Gnanapavan\*, Joseph A. Sparano\*,  
 Jay B. Shah\*, Alex W. van Rhijn\*, Steffen Ditschuneck\*, Philipp E. Spiess\*, Peter C. Black\*

## Current Guidelines

### Multicenter Assessment of Neoadjuvant Chemotherapy for Muscle-invasive Bladder Cancer

#### RESULTS

Variable	Odds regression analysis	
	HR (95% CI)	p-value
Age, yr	0.99 (0.98-1.01)	0.67
Time between NAC and BC	0.99 (0.98-1.01)	0.92
Gender		
Female	1	
Male	1.15 (0.76-1.76)	0.49
Chemotherapy regimen		
MIVAC	1	
GC	1.25 (0.80-1.93)	0.34
Other regimen	1.64 (1.01-2.66)	0.04
Statistical margin		
Negative	1	
Positive	2.21 (1.36-3.57)	0.001
Lymph node dissection		
None	1	
Standard	1.25 (0.36-3.54)	0.72
Extended	1.65 (0.48-5.93)	0.42
pPR (pT1N0)	1	
Yes	0.25 (0.16-0.40)	<0.001
No		

Herrington Ziegler\*, Patrick N. Eggen\*, Adrian S. Poincy\*, Laura S. Merritt\*,  
 Colin P. Dwyer\*, Maria C. Alar\*, Lorenz-Maria Kreibitz\*, Mikko S. Koskela\*,  
 Peter V. Van\*, David Vignaud\*, Francesco Vignaud\*, Nicholas J. Compton\*, William Kattan\*,  
 Alan A. Chalfant\*, Joelle S. Gagnon\*, Christel E. Gagnon\*, James Cunningham\*,  
 John A. McCreedy\*, Jonathan Anagnostou\*, Shabbir F. Shariat\*, Jonathan E. Wright\*,  
 Andrew C. Thompson\*, Todd M. Morgan\*, Jeff M. Hollender\*, Timothy J. Brannan\*,  
 John H. Kim\*, Michael A. Brennan\*, Paul Gnanapavan\*, Joseph A. Sparano\*,  
 Jay B. Shah\*, Alex W. van Rhijn\*, Steffen Ditschuneck\*, Philipp E. Spiess\*, Peter C. Black\*

## No residual disease (pT0)

Table 2. Cystectomy, chemotherapy and pT0 in treatment and control arms

	Nests 1*	Nests 2*	SNAC†	MIVAC‡	Stata
No. M:Control intent to treat	151/160	155/154	153/154	491/487*	950/950
No. R:Control No. (%)	284 (11.8)	271 (20.8)	250 (20.8)	484 (9.8)	1,287 (13.6)
CC	120 (10.8)	120 (10.8)	120 (10.8)	250 (20.8)	630 (6.7)
Control	164 (10.8)	151 (10.8)	130 (10.8)	234 (10.8)	657 (7.0)
No. M: pT0 intent to treat	158	158	158	395	768
No. pT0 intent to treat	33 (33.0)	37 (40.0)	48 (30.0)	57 (29.0)	165 (21.0)
CC	17 (33.3)	18 (33.3)	18 (33.3)	26 (33.3)	77 (35.0)
Control	16 (30.0)	19 (33.3)	30 (33.3)	31 (33.3)	88 (40.0)

- ✓ 5-15% TURB alone
- ✓ 25-50% NAC

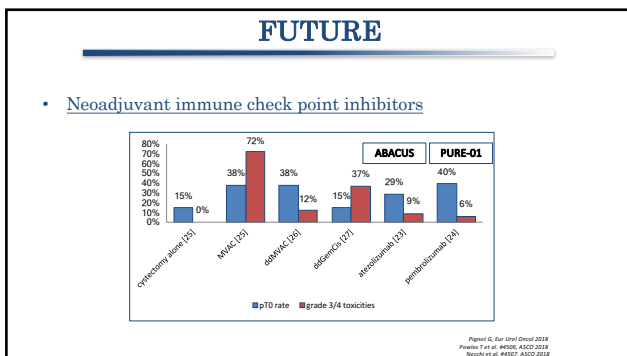
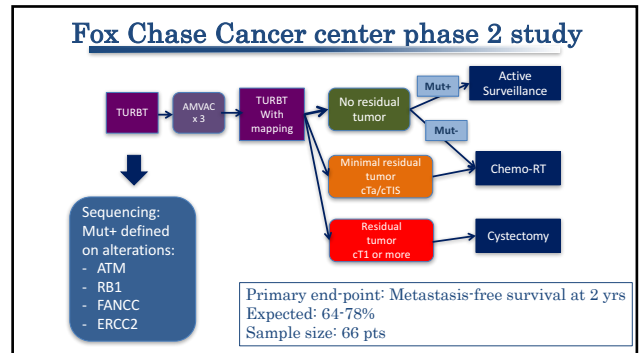
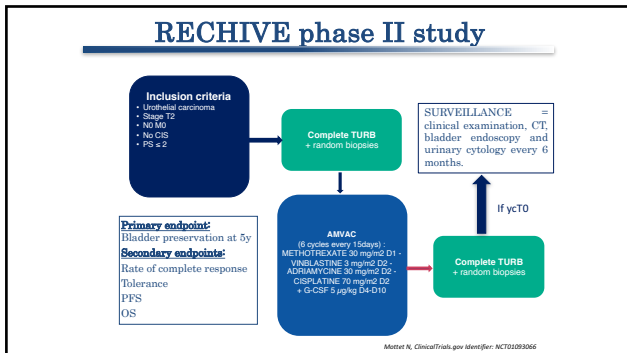
Lavery et al. = Pathological T0 Following Radical Cystectomy with or without Neoadjuvant Chemotherapy: A Useful Surrogate.

## Outline

- ✓ Neoadjuvant chemotherapy is the standard of care.
- ✓ No residual disease = surrogate of overall survival.
- ✓ Outcomes of patients with no residual disease after TURB and neoadjuvant chemotherapy without local treatment.
- ✓ Ongoing trials and future.







### Conclusions

**Management of favourable outcomes after neoadjuvant chemotherapy**

- ✓ Neoadjuvant chemotherapy and cystectomy is the standard of care.
- ✓ pT0 = surrogate of overall survival.
- ✓ Radical cystectomy mandatory in case of pT0 ?
- ✓ Immune check point inhibitors.

HOPITAL UNIVERSITAIRES PARIS NORD - VAL DE SEINE

Université de Paris

### Management of favorable outcomes after neoadjuvant chemotherapy

**you** Young Academic Urologists

**EAU** European Association of Urology

**Evangelos Xylinas, MD, PhD, FEBU**  
 Associate Professor of Urology  
 Bichat-Claude Bernard Hospital  
 Paris Descartes University, France