



Urothelial recurrences in patients with invasive urothelial cancers

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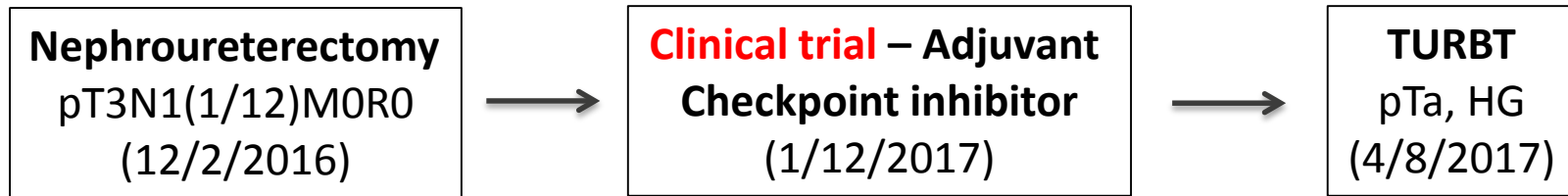


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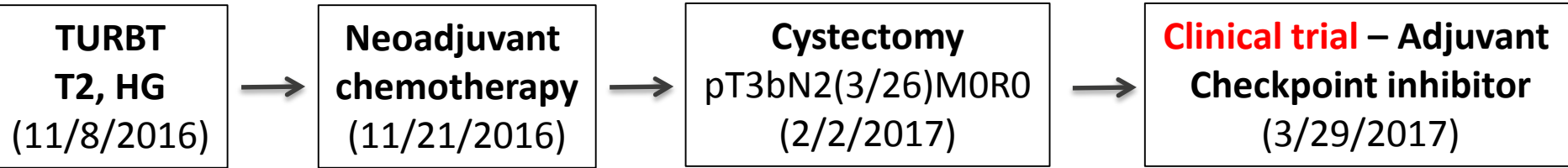
Scenario 1: the NMIBC recurrence



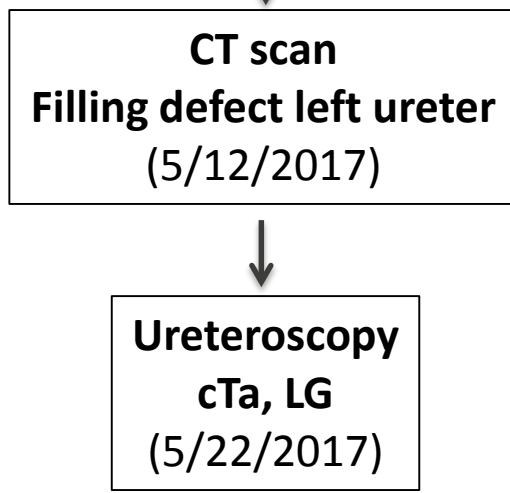
- Did the patient fail the clinical trial?
- If not, can they get BCG?
 - What about synergistic toxicity?
 - What about synergistic efficacy?
 - Will biomarkers be affected (if assessed)?



Scenario 2: the upper tract recurrence



- Did the patient fail the clinical trial?
- If not, nephroureterectomy?
 - What about synergistic toxicity?
 - What about treatment interruption?
 - Will biomarkers be affected (if assessed)?





Defining treatment failure is important

- Urothelial recurrences are common
 - The entire urothelium is at risk
 - Do they always represent a treatment failure?
- “Treatment failure” has consequences
 - Experimental treatment usually stops
 - Risk group changes (e.g., 1st vs 2nd line)
 - Options shrink
- Consistency is an important goal
 - Does your treatment failure definition vary?



How common are urothelial recurrences?

		Primary tumor		
		Bladder (RC)	Bladder (ChemoRT)	Upper tract
Recurrence location	Bladder	-	15% \leq T1 20% \geq T2	30%
	Upper tract	5%	?	5%
	Urethra	4%	?	<1%

Gaskis et al. Eur Urol 2017; Picozzi et al. J Urol 2012; James et al. NEJM 2012
Shiple et al. Urology 2002; Weiss et al. Int J Rad Onc Biol Phys 2008; Seisen et al. Eur Urol 2015



Urothelial recurrences after cystectomy

	Upper tract	Urethra
Detected by screening	1/3 (imaging)	1/3 (cytology)
Time to recurrence	3 years	1 year
Urothelium only	90%	65%
+ metastases	10%	20%
+ pelvic disease	5%	10%
Outcome @ 5y	55% die	45% die



Predictors of recurrence after cystectomy

Upper tract		Urethra
Multifocality		
Tis/Ta/T1		
T4		
(ureter)	Positive margin	(urethra)

Gaskis et al. Eur Urol 2017; Kim et al. PLoS One 2014; Picozzi et al. J Urol 2012
Boorjian et al. Eur Urol 2011; Umbreit et al. Cancer 2010



Urine tests affect recurrence detection

- Upper tract
 - Positive urine test + negative cystoscopy = more testing (imaging, retrogrades, ureteroscopy)
- Urethra
 - Positive urethral wash = more testing (imaging, biopsy, urethrectomy)
- Implication: standardization required to avoid bias
- Guideline levels of evidence are low (opinion)



Bladder recurrences after chemoradiation

- Two patterns:
 1. Muscle invasive (20%)
 - Early, old tumors resistant to therapy
 2. Non-muscle invasive (15%)
 - Later, ? new tumors
- Predictors of recurrence
 - Incomplete TURBT, \geq T3, hydronephrosis, CIS



Bladder recurrence after upper tract resection

- Median time = 2 years
- 55% \leq T1 and 45% \geq T2
- Predictors of recurrence:
 - Patients: male, history of BC, CKD
 - Tumor: ureter (vs renal pelvis), multifocal, \geq T2
 - Procedure: laparoscopic, postop instillation



Technique affects recurrence detection

- Enhanced endoscopy is better
 - Blue light (Cysview)
 - Narrow band imaging
- Random bladder biopsies?
- Implication: endoscopy standardization required on trial to avoid bias



How to define treatment failure on trial?

- Option 1 (a.k.a. the pessimist)
 - Any urothelial recurrence = progression event
 - Implication: urothelial recurrence pulls you off study
- Option 2 (a.k.a. the optimist)
 - Urothelial recurrence = recurrence event
 - Invasive urothelial recurrence ($\geq T2$) = progression event
 - Implication: can treat $\leq T1$ and remain on trial



Thank you for your attention



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