

Evaluation of the UroVysion™ Test in Predicting Recurrence and/or Progression of Disease in Patients Receiving initial BCG for Primary High Grade Ta-T1 and CIS Urothelial Carcinoma of the Bladder

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Introduction

- Patients diagnosed with high grade non-muscle invasive bladder cancer (NMIBC) and treated with BCG remain at risk for recurrence and progression of disease.
- The UroVysion FISH assay (UroVysion) has been reported to predict response to BCG therapy.
- Herein, we validated the association of UroVysion results with BCG-naïve patients at risk of subsequent disease recurrence/progression.

Materials and Methods

- We performed a multi-center prospective study that enrolled patients with primary high grade Ta-T1 tumors, CIS or recurrent NMIBC who initiated BCG therapy.
- UroVysion testing was performed on urine specimens collected prior to the first instillation of BCG therapy, at time of the 6th instillation, and at 3-month surveillance.
- Clinicians were blinded to the UroVysion results for specimens collected pre-BCG and at the 6th instillation of BCG therapy
- Patients were monitored for disease recurrence by cystoscopy following standard of care intervals.
- Follow up data were collected at time of recurrence or progression and/or at 3 months, 6 months, and 9 months.

Results

- The study included 151 patients (80% men) with stages of Ta (42%), T1 (25.8%), CIS alone (17.9%), Ta+CIS (2%), and T1+CIS (7.3%).
- At baseline, 43.9% (65/148) were UroVysion positive.
- There were 46 events, including 36 recurrences and 10 progressions.
- KM survival curves demonstrate significant reduced event free survival for UroVysion positive tests at baseline, 6-week and 3 months (Figure).
- Patients with a positive UroVysion test at baseline prior to BCG or at 6 week instillation were more likely to experience recurrence or progression at 6 months and 9 months but differences at 3 months were not statistically significant.

Patient Characteristics

Attribute	Classification	Total	FISH Positive @ Baseline	FISH Negative @ Baseline	Chi Square	p-Value
	Total	148 (116 + 32)	65/148 (43.9%)	83/148 (56.1%)	4.378	0.0364
	Uninformative	3				
Age	Range	27 - 93				
	Mean	70.1				
	Median	71				
	Std. Deviation	10.83				
Gender	Male (2 uninform)	121/151 (80.1%)	50/121 (41.3%)	69/121 (57.0%)	5.969	0.0146
	Female (1 uninform)	30/151 (19.9%)	15/30 (50.0%)	14/30 (46.7%)	0.067	0.7961
	Uninformative	3				
Stage	CIS (2 uninform)	27/151 (17.9%)	18/25 (72.0%)	7/25 (28.0%)	9.680	0.0019
	Ta (1 uninform)	64/151 (42.4%)	17/63 (27.0%)	46/63 (73.0%)	26.698	<0.0001
	T1 (with Ta/T1)	39/151 (25.8%)	19/39 (48.7%)	20/39 (51.3%)	0.051	0.8208
	CIS/Ta Dual Dx	3/151 (2.0%)	1/3 (33.3%)	2/3 (67.7%)	0.667	0.4142
	CIS/T1 Dual Dx	11/151 (7.3%)	8/11 (72.7%)	3/11 (27.3%)	4.545	0.0330
Grade	Unknown (1) / Unspecified (6)	7/151 (4.6%)	2/7 (28.6%)	5/7 (71.4%)	2.571	0.1088
	Uninformative	3				
	High (3 uninform)	141/151 (93.4%)	64/148 (43.2%)	74/148 (50%)	1.419	0.2336
	Low	7/151 (4.6%)	1/148 (0.68%)	6/148 (4.1%)	7.143	0.0075
	Unspecified	3/151 (2.0%)	0/148 (0.0%)	3/148 (2.0%)	6	0.0143
	Uninformative	3				

All 7 Sites Combined (N=148)	3 Months	6 Months	9 Months
Recurrence Rate	21/148 (14.2%)	32/148 (21.6%)	36/148 (24.3%)
Progression Rate	5/148 (3.4%)	9/148 (6.1%)	10/148 (6.8%)
Total Events	26/148 (17.6%)	41/148 (27.7%)	46/148 (31.1%)

FISH at Baseline (Prior to Initial BCG)

			Combined Events at 3 Months	Combined Events at 6 Months	Combined Events at 9 Months	p value (FISH+ vs FISH neg) @ 3 Months	p value (FISH+ vs FISH neg) @ 6 Months	p value (FISH+ vs FISH neg) @ 9 Months
FISH +	65		15/65 (23.1%)	28/65 (43.1%)	29/65 (44.6%)	0.1191	0.0002	0.0016
FISH -	83		11/83 (13.3%)	13/83 (15.7%)	17/83 (20.5%)			

FISH at time of the 6th instillation

			Combined Events at 3 Months	Combined Events at 6 Months	Combined Events at 9 Months	p value (FISH+ vs FISH neg) @ 3 Months	p value (FISH+ vs FISH neg) @ 6 Months	p value (FISH+ vs FISH neg) @ 9 Months
FISH +	41		10/41 (24.4%)	18/41 (43.9%)	18/41 (43.9%)	0.1839	0.0035	0.0210
FISH -	88		13/88 (14.8%)	17/88 (19.3%)	21/88 (23.9%)			

FISH at 3 month Surveillance

			Combined Events at 3 Months	Combined Events at 6 Months	Combined Events at 9 Months	p value (FISH+ vs FISH neg) @ 3 Months	p value (FISH+ vs FISH neg) @ 6 Months	p value (FISH+ vs FISH neg) @ 9 Months
FISH +	35		10/35 (28.6%)	17/35 (48.6%)	18/35 (51.4%)	0.0393	0.0003	0.0014
FISH -	79		10/79 (12.7%)	13/79 (16.5%)	17/79 (21.5%)			

Conclusions

- Approximately one-third of patients who initiate BCG have recurrence or progression events within 9 months of diagnosis.
- A positive UroVysion assay at baseline and at the conclusion of BCG therapy was associated with a **significantly** increased likelihood of experiencing such an event at 6 and 9 months.
- These data may be utilized for guiding management as well as clinical trial enrollment.

