



## Shining a Light on Rare Forms of Bladder Cancer

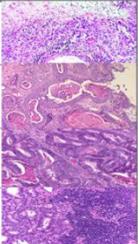
### Meet our Presenter

**Dr. Andrea Apolo:** Dr. Apolo is a Medical Oncologist and the Chief of the Bladder Cancer Section of the Genitourinary Malignancies Branch of the National Cancer Institute. Dr. Apolo received her MD from Albert Einstein College of Medicine in New York. And she completed an Internal Medicine Residency at New York-Presbyterian Hospital. She followed up with a Medical Oncology Fellowship at Memorial Sloan Kettering Center. And then she joined the Medical Oncology Branch of the National Cancer Institute, in charge of Bladder Cancer Translational Program. She holds Board Certifications for Internal Medicine and Medical Oncology. Dr. Apolo has served in national, international committees including the Genitourinary Tract Leader of the Education Program Committee and a member of the Scientific Program Committee of the American Society for Clinical Oncology. She's a member of the Bladder Cancer Program Committee of the Society of Urologic Oncology, and is a member of the BCAN Scientific Advisory Board. Dr. Apolo is very interested in identifying molecular alterations in tumors that will serve as targets for individualized treatment strategies. Thank you so much Dr. Apolo for joining us today.

### Introduction

**Dr. Apolo:** Thank you for having me, and it is really a great pleasure for me to really highlight the issues and the ongoing effort in rare bladder cancers. This is an area that I am very interested in because as a tertiary center here at the NIH, we see a lot of rare tumors, and the treatments are limited. So what I'm going to do today is I'm going to talk about what these rare tumor are, what are the efforts ongoing right now, what do we know about them in terms of prognosis, in terms of treatment, in terms of diagnosis. And there's really two groups that I'm going to talk about. I'm going to talk about the pure rares that are not urothelial carcinoma, that make up the other 10% of urothelial carcinoma histology. And I'm going to talk about the urothelial carcinoma histologies that are mixed, that have rare components in them, and therefore these tumors behave differently.

### Bladder cancer Histology

Urothelial Carcinoma	90%	
Squamous Cell Carcinoma	5%	
Adenocarcinoma	0.5-2%	
Small Cell Carcinoma	<1%	

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**Dr. Apolo:** So urothelial carcinoma is the predominant histology for bladder cancers, but there are other histologies such as squamous cell carcinoma, adenocarcinoma, and small cell carcinoma. When we talk about treatments for bladder cancer, we really talk about treatments for urothelial carcinoma. So, all the new FDA approvals, all of the clinical trials, these are all patients with urothelial carcinoma. The rare tumors, they're too uncommon to enroll in clinical trials in a perspective manner or in a randomized manner. There are just not enough

patients. So we do lack evidence in terms of the best treatment options for these patients, and that's what I'm going to highlight today. In terms of the presentation for rare bladder tumors, the presentation is similar to urothelial carcinoma tumors in that they present with painless hematuria. This can be gross visible hematuria; blood in the urine, or microscopic that's picked up by a doctor's office. Also, there can be voiding symptoms; symptoms when you urinate such as frequency, urgency, or pain with urination.

### Common presentation of rare bladder tumors

- Similar to urothelial carcinoma, patients with rare bladder tumors initially present with:
  - Painless hematuria
    - grossly visible
    - microscopic
  - Irritative voiding symptoms
    - Frequency
    - Urgency
    - dysuria

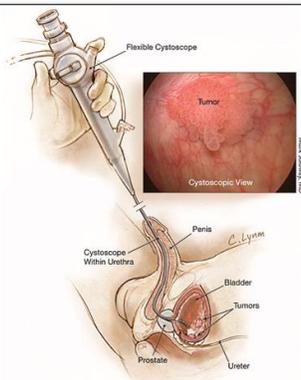


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### Detection of rare bladder tumors

- Similar to urothelial carcinoma, patients with rare bladder tumors are initially evaluated with:
  - A cystoscopy and if indicated a Transurethral Resection of Bladder Tumor (TURBT) of the bladder is a surgical procedure that is used both to diagnose bladder cancer and to remove cancerous tissue from the bladder
  - Imaging, such as a CT of the chest, abdomen, and pelvis and if indicated a needle biopsy

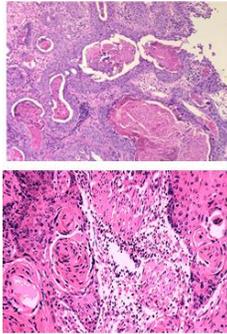


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In terms of how it's initially evaluated, it's managed similar to urothelial carcinoma. The bladder in that, generally a urologist looks inside the bladder using a cystoscope. And if it's appropriate, and they see a tumor, they may do a transurethral resection of the bladder tumor, something that we call a TURBT. And this is both diagnostic and also therapeutic. In a more advanced disease, imaging may be done with a CT of the chest, abdomen, and pelvis. And if a mass is found, often a needle biopsy is performed.

## Squamous Cell Carcinoma of the bladder

- 1.2-5% of bladder carcinoma in western countries
  - >50% in schistosomiasis endemic areas (75% in Egypt)
- Predisposing factors include:
  - Chronic urinary tract infections
  - Spinal cord injury with indwelling catheters
  - Urinary tract calculi
  - Prior pelvic radiation
- Mean age 68 years
- Male predominance



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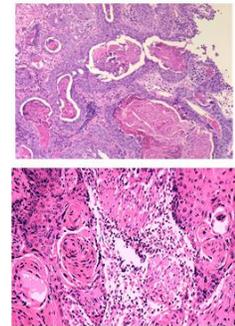
So we'll start off with squamous cell carcinoma of the bladder. And these account for 5% of the rare bladder cancer tumors. So, squamous cell carcinoma accounts for about 1.2 to 5% of bladder carcinomas in the Western countries. It is associated with infection, with schistosomiasis, which is endemic in the Nile River Valley in Africa. And cases of bladder cancer are very high in Egypt, and they're associated with this parasite. Here in the United

States, this is very rare and not a risk factor. Generally the predisposing risk factors for squamous cell carcinoma of the bladder are chronic urinary tract infections, patients with spinal cord injury that have indwelling catheters, urinary tract stones, prior pelvic radiation. The median age for squamous cell carcinoma is 68, and similar to urothelial carcinoma, there's a male predominance.

So, squamous cell carcinoma often present with advanced stage. These are high grade, and they do have a high rate of muscle invasion; only about 2.6% of these presents as non-muscle invasive disease. About 20% of the time, these patients already have lymph node involvement at presentation. But they do have a lower rate of distant metastases. These tumors tend to spread locally, and generally causing issues with local blockage or pain. And when they're treated and they recur, so that the patient has the bladder removed and the cancer comes back, these generally come back locally, not with distant metastases as urothelial carcinoma can happen with metastases in other organs. This is generally a local spread. Next slide.

## Squamous Cell Carcinoma of the Bladder

- Often advanced stage with high grade and high rate of muscle invasion (only 2.6% non-muscle invasive)
- Lymph node involvement (20%)
- Lower rate of distant metastases (8-10%)
- 90% of deaths due to local regional recurrence
  - About 75% of patients will recur locally

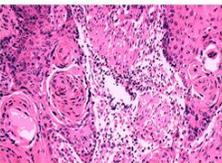
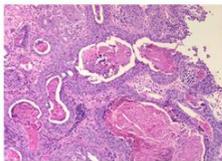


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So, for patients with non-muscle invasive disease and squamous cell carcinoma, early cystectomy is advised because these tumors just don't respond to chemotherapy. Radiation is effective and may be appropriate in some patients

## Squamous Cell Carcinoma of the Bladder

- Early cystectomy for non-muscle invasive disease given high local recurrence and poor response to chemotherapy
  - Consider neoadjuvant or adjuvant radiation therapy
- Systemic therapy not proven to be efficacious
  - Gemcitabine/Cisplatin and ifosfamide/paclitaxel/cisplatin (ITP) showed a ~24% response rate without improved overall survival



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undergoing surgery. And that can happen either before the surgery, called neoadjuvant radiation, or after the surgery, called adjuvant radiation, in certain patients. The systemic therapy with chemotherapy, although it has shown to have some response in terms of shrinking of the tumor, we haven't seen improvement in survival with chemotherapy. So it may be good for symptom control. And we use regimens similar to those used for urothelial carcinoma. And these include Gemcitabine and Cisplatin.

Another regimen that has been tested

in rare tumors is ITP. And that stands for ifosfamide, paclitaxel, cisplatin. That's a combination of chemotherapy. And both of these regimens show about 24% response in the first-line setting.

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