Review

Managing and Preventing Progression in Patients with Mid- to High-Risk Bladder Cancer: A Case Study Approach

Dr. Soloway uses a case study approach to engage symposium participants in a lively discussion about various aspects of managing and preventing progression in patients with mid- to high-risk tumours. This session stimulated an exchange of ideas and best practices.

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Dr. Soloway is Chairman of the Department of Urology at the University of Miami, Miami, Florida, USA. His research, teaching, and clinical careers are shaped by his desire to translate laboratory findings to cutting-edge patient care. He has developed a model for bladder cancer, has collaborated on seminal clinical studies of prostate cancer, and has been involved in the advancement of new technologies to diagnose urologic cancers. His work in advancing the practice of urology has been recognised with the prestigious Gold Cystoscope Award.

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Case 1: Bacillus Calmette-Guérin in High-Risk Patients

SOLOWAY: The first patient is a 53-year-old man who had a history of urothelial cancer. He underwent a transurethral resection of bladder tumour (TURBT) for a T1 high-grade tumour followed by bacillus Calmette-Guérin (BCG) but no maintenance in May 2003 at another institution. I saw him 8 mo later. The original area was biopsied and was negative but on completion of the transurethral resection (TUR), I saw this small lesion on the anterior wall, which was biopsied and revealed high-grade T1a. So, Prof Rischmann what would you do?

RISCHMANN: The question here is whether this is a BCG failure or inadequate initial immunotherapy. This patient is at risk of progression so he must be informed of this and I would not wait for more invasive disease before recommending a cystectomy. The other option is to continue BCG therapy with maintenance but follow him very closely.

SOLOWAY: So let me ask the audience, is it reasonable to try again with BCG?

AUDIENCE: 85% said another trial of BCG and 15% said cystectomy.

SOLOWAY: We have a reasonable consensus. I elected also to give him full-dose BCG with interferon and so far he has been free of disease for 18 mo. I’m not sure if the interferon is beneficial but there are some data on this subject. Interestingly I did not use maintenance but I think it is a good idea to do so. A brief question to the audience: For a T1 high-grade tumour do you give one-dose intravesical chemotherapy at the time of TUR?

AUDIENCE: 100% for single-shot chemotherapy at the time of TUR

SOLOWAY: So we’re all believers in one-dose chemotherapy at TUR. How many in the audience will give him at least 1 yr of maintenance BCG? Again virtually 100%. I want to highlight two recent publications concerning BCG failures in high-risk patients. The first is from Dr Palou of Barcelona in which 62 patients with Ta, T1, or carcinoma in situ (CIS) were treated but not with maintenance BCG or a re-TUR. Cystectomy was done for recurrent high-grade disease and 6% of these patients had positive lymph nodes and 5-yr disease-specific survival was only 79% [1]. Also, if urothelial carcinoma was present in the prostate, the disease-specific survival was only 38%. A similar analysis at the University of Miami in 90 patients revealed 12% positive lymph nodes and the disease-specific survival was only 65% [2]. So it’s a word of warning when using BCG in high-risk patients.

Given that scenario let me ask Dr Böhle about a patient.

Case 2: Treatment Options for Recurrent High-Risk Tumours

SOLOWAY: This patient had CIS followed by full-dose BCG for 6 wk and maintenance for 1 yr; then he stopped treatment. One year later he had high-grade papillary T1.

BÖHLE: We know that the immune response wanes with time. So the non-maintenance of 1 yr might be the reason but still from the clinical viewpoint, I think this patient has a very high risk of progressing further and he may be one of those patients with positive nodes. In this case I would recommend cystectomy.

AUDIENCE:

50% cystectomy
0% BCG and interferon
50% re-TUR and BCG

PALOU: From our experience in earlier failures if you give some more BCG, treatment fails again, but after 1 or 2 yr we also can consider this as a new tumour and retreat patients with BCG. However, we also must advise the patient that he is at a higher risk compared with the beginning. So I would give another course of BCG in this patient.

LAMM: Well, there is no right or wrong choice and either is acceptable. I would present both options to the patient and I would also look at the specimen with a pathologist. If the tumour characteristics look good and the patient is willing to accept the risk then I would say that BCG would be fine.

RISCHMANN: I agree. This patient had CIS treated with BCG and now has T1 disease so to me this represents a kind of progression. If he had maintenance therapy and disease recurred on BCG then this certainly is an indication for cystectomy.

SOLOWAY: In my personal view any high-risk, high-grade T1 tumour after an initial trial of BCG even
with a hiatus, I would err on the side of an earlier cystectomy. But, again, as Dr Lamm indicated there is no right or wrong answer.

Dr Palou when do you biopsy the prostatic urethra? What are the indications of transurethral resection biopsy of the prostatic urethra in patients with high-grade urothelial tumours?

PALOU: In primary Ta or T1 or each time there is a recurrence we do cold cup biopsies with just two bites of the prostatic urethra. In those cases with CIS of the prostatic urethra or with prostatic involvement we do a TUR biopsy of the prostatic urethra. In our series when there is CIS in the bladder, 10% of these will also have CIS in the prostatic urethra.

**Case 3: Management of BCG Failures**

SOLOWAY: The last case is a 49-year-old obese man with a history of smoking. In 2001, he was treated for primary CIS of the bladder with TUR followed by two 6-wk courses of BCG but no maintenance. A repeat biopsy in May 2003 by the first urologist and then by myself later that year showed no cancer. I gave him some maintenance BCG and a rebiopsy a few months later revealed recurrent CIS. Now we are aware of O’Donnell’s work with BCG and interferon for BCG failures, which according to him show a short-term 50% response rate. So should this patient have this option or should he undergo a cystectomy?

RISCHMANN: This man has failed two courses of BCG so there’s no benefit to a third course or further maintenance. I have no experience with interferon and I consider this patient a BCG failure so I would recommend a cystectomy.

SOLOWAY: Let's see what the audience thinks.

**AUDIENCE:** 98.2% in favour of cystectomy

SOLOWAY: I thought the same as the audience and did a cystectomy. Now the prostatic urethra looked normal so would you perform an orthotopic neobladder?

RISCHMANN: I think it is important to have some prostatic tissue from the TUR to see if the prostate is involved and, if so, whether it is in the stroma, duct, or urethra.

SOLOWAY: Good point. This fellow had a cystoprostatectomy and the nodes were negative. He had residual CIS but he also had muscularis propria invasion in the prostate with involvement of the glands, stroma, and seminal vesicle. So I did an ileal conduit rather than an orthotopic diversion followed by systemic chemotherapy. He is at risk for a urethral recurrence and unfortunately his long-term prognosis is not great. Thank you everyone.

**References**
