EMDA- Electromotive Drug Administration + BCG

Innovative approach from Italy improves efficacy of sequential BCG and Mitomycin C

Immunotherapy with BCG has become standard of care for high grade, non invasive bladder tumors, and has been shown to have a positive influence on recurrence and progression, while intravesical chemotherapy with various drugs has consistently demonstrated reduction in short-term tumor recurrence rates but no impact on disease progression. Intravesical treatments using chemotherapy drugs are limited because the effects wear off within two years.

BCG treatments followed by a novel delivery system using electromotively delivered Mitomycin C are showing some of the most surprising recurrence-free response rates ever seen in superficial bladder cancer treatments.

Sequential BCG and electromotive mitomycin (EMDA) versus BCG alone:

disease-free interval 69 months vs. 21 months

recurrence rates: 41.9% vs 57.9

progression 9.3% vs 21.9%

overall mortality 21.5% vs 32.4%

disease-specific mortality 5.6% vs 16.2%

Side-effects were mainly localised to the bladder.1

Lead investigator SM Di Stasi reports that after ten years of using this technique, systemic side effects are not a problem.

Mitomycin C followed by electromotive drug administration/EMDA is more able to penetrate the bladder lining. Experimental and clinical reports demonstrate that electric current significantly increases the transport of mytomicin.

INTERPRETATION: BCG-induced inflammation might increase the permeability of the bladder mucosa such that mitomycin can reach the target tissue more easily and exert its anticancer effect.

U.S. experts from MD Anderson wrote in a recent review, "Could the addition of BCG (which causes local inflammation) increase the absorption of mitomycin such that the added benefit is, in part, due to systemic exposure to low-dose (‘metronomic’) chemotherapy? This would explain the rather remarkable improvement in disease specific mortality (almost 3 fold, from 16.2% to 5.6%) seen in patients receiving combination therapy."2

Open questions remaining: The study considered a recurrence of CIS at 3 month as a BCG failure, but this may not be true as BCG can take longer than 3 months to exert its full effects, thus the recurrence rate of 71.4% of those using BCG alone may be falsely elevated; Maintenance BCG was not used, thus the BCG arm may have been sub-optimal. Still, the review concludes, "Electromotive mitomycin C appears to enhance the efficacy of intravesical BCG without significant increase in side effects, and warrants further validation."2

Experts in Italy have been working with Physion, the company that designed the electromotive drug delivery system. From the Physion site, "EMDA utilizes an electrical current to impart an accelerated, directional (towards the tissues) movement of ionized drugs in an intravesical solution, which results in greater quantities of drugs being delivered to greater tissue depths than is achievable by passive diffusion. Furthermore, the rate of drug administration is fully controllable simply by varying the intensity of the electric current."

1.Sequential BCG and electromotive mitomycin versus BCG alone for high-risk superficial bladder cancer: a randomised controlled trial. * Di Stasi SM, * Giannantoni A, * Giurioli A, * Valenti M, * Zampa G, * Storti L, * Attisani F, * De Carolis A, * Capelli G, * Vespasiani G, * Stephen RL. Department of Surgery/Urology, Tor Vergata University, Rome, Italy. Lancet Oncol. 2006 Jan;7(1):43-51. PMID: 16389183

2.A combination of intravesical and BCG electromotive mitomycin for high-risk superficial bladder cancer; Ashish M Kamat* and Colin PN Dinney Correspondence *Department of Urology, Unit 1373, University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030-4009, USA Nature Clinical Practice Urology (Nov. 2006) 3, 472-473 doi:10.1038/ncpuro0559