

A PHASE II STUDY OF GEMCITABINE PLUS CISPLATIN CHEMOTHERAPY IN PATIENTS WITH MUSCLE-INVASIVE BLADDER CANCER WITH BLADDER PRESERVATION FOR THOSE PATIENTS WHOSE TUMORS HARBOR DELETERIOUS DNA DAMAGE RESPONSE (DDR) GENE ALTERATIONS

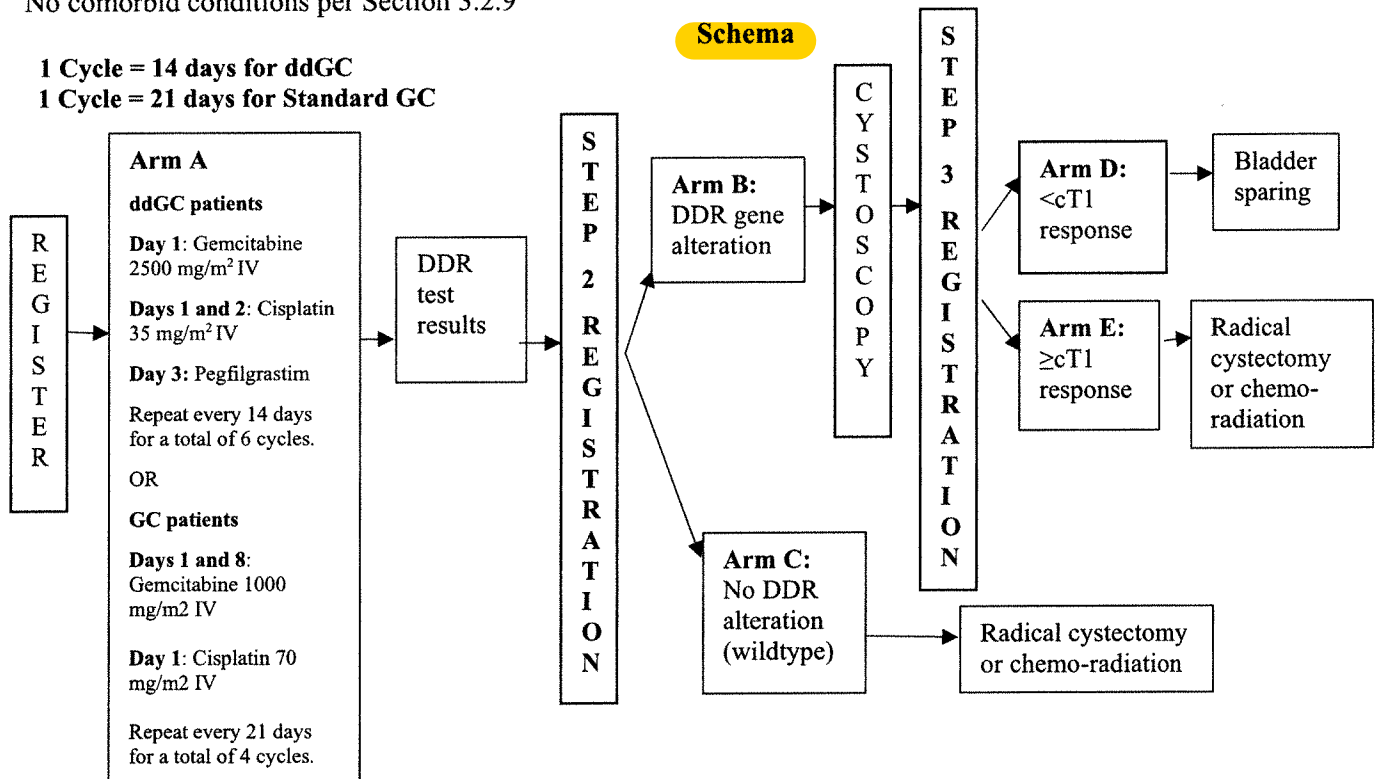
Eligibility Criteria (see Section 3.0)

Histologically confirmed urothelial carcinoma of the bladder
 10-20 unstained slides or 1 FFPE block from pre-treatment TUR available
 Clinical stage T2-T4aN0/xM0
 Candidate for radical cystectomy
 No prior systemic chemotherapy or radiation therapy for the bladder
 No major surgery or RT ≤ 4 weeks
 Non-pregnant and non-nursing
 Age ≥ 18 years
 ECOG PS = 0-1
 No comorbid conditions per Section 3.2.9

Required Initial Laboratory Values

Absolute neutrophil count (ANC): ≥ 1000/mm³
 Platelet count: ≥ 100,000/mm³
 Calc. creatinine clearance: ≥ 55 mL/min
 Total bilirubin: ≤ 1.5 x ULN
 (For patients with documented Gilbert's syndrome Bilirubin ≤ 3 x ULN)
 AST/ALT: ≤ 2.5 x ULN
 Alkaline phosphatase: ≤ 2.5 x ULN

1 Cycle = 14 days for ddGC
 1 Cycle = 21 days for Standard GC



Chemotherapy is to continue for 6 cycles or unacceptable adverse events (at least 4 cycles must be given for patients to proceed to Step 2 registration). Patients on the standard treatment (gemcitabine on days 1 and 8 and cisplatin on day 1) must receive 4 cycles to proceed to Step 2 registration. Patients will be followed for five years after completion of chemotherapy or radical cystectomy, or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.