Guy's and St Thomas' NHS
NHS Foundation Trust

CLINICAL TRIAL OF AN INVESTIGATIONAL MEDICINAL PRODUCT (CTIMP)

END OF STUDY REPORT TO MHRA

1. Details of Chief Investigator

Name:	Mr. T. S O'Brien
Address:	Urology centre, Southwark wing, Guy's Hospital, St. Thomas' Street SE1 9RT
Telephone:	0207 1886796
E-mail:	Tim.OBrien@gstt.nhs.uk
Fax:	0207 1886798

2. Details of study

Full title of study:	A randomised Study of "bluelight" hexyl amino levulinic acid (HAL) photodynamic assisted resection of bladder tumours versus conventional "white light" transurethral resection of newly diagnosed bladder tumours comparing rates of tumour recurrence over one year – A phase IV trial.
Name of main REC:	East London and the City REC
REC reference number:	04/Q0603/42
Date of favourable ethical opinion:	06 Jan 2005
Sponsor:	Guy's and St. Thomas' NHS Foundation Trust
EudraCT Number:	2004-002760-16
Single Centre	Guy's Hospital

3. Commencement and completion dates in the UK

Commencement	3rd March 2005
Completion	10th June 2011

4. Study Design

249 patients enrolled at a single centre, between March 2005 and April 2010 into a randomised trial of Hexvix assisted blue-light (B/L) TURBT plus single shot intravesical MMC versus white-light (W/L) TURBT plus single shot MMC. All patients had suspected non-muscle invasive bladder cancer (NMIBC) based on appearance at flexible cystoscopy or imaging. Patients with a previous history of bladder cancer were excluded.

5. Study Objectives

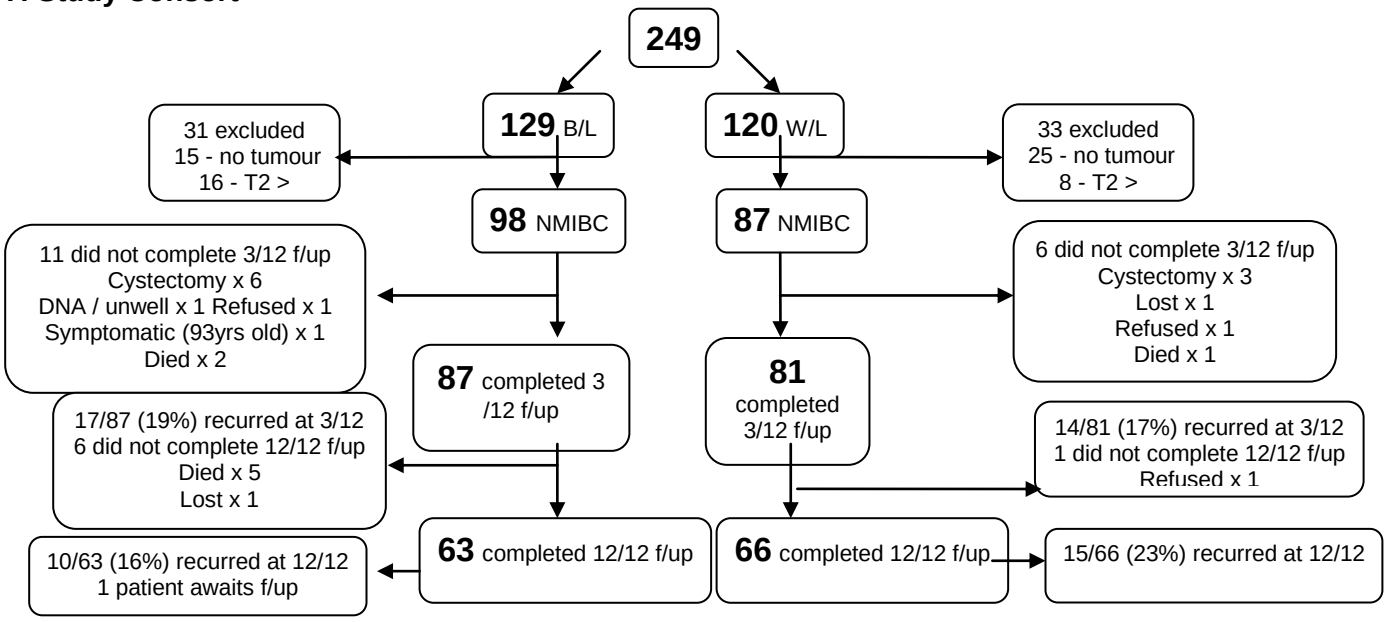
Primary endpoints: tumour recurrence within 3/12 and at 12/12 post initial TURBT (pearson chi square).

6. Study Design

129 patients randomised to B/L and 120 to W/L. 183 (73%) patients were male; mean age 68 (range 29-95); 201 (80%) presented with macroscopic haematuria.

In 207/249 (83%) histology revealed cancer, and in 184/207 (89%) the diagnosis was NMIBC (B/L 99: W/L 85). Final TNM classification was low grade/G1pTa =98 (B/L 50: W/L 48); high grade/G3pTa = 28 (B/L 13: W/L 15); high grade/G3pT1=57 (B/L 35:W/L 22). Primary CIS was seen in one patient and secondary CIS in 37 (B/L 25:W/L 12). 128/184 (70%) patients received single dose MMC (B/L 62: W/L 66). MMC was not administered to 56 (30%) patients due to concerns about the safety of intravesical MMC after a deep resection. 8/184 (4%) (B/L 5: W/L 3) patients did not undergo a cystoscopy within 3/12 (3 died, 2 refused, 2 lost, 1 discharged). There was no statistically significant difference in recurrence between the 2 arms at 3 or 12 months. 3/12 recurrence: 17/94 (18%) B/L vs 14/82 (17%) W/L (p=0.86). By november 2010, of those 145 patients (B/L 77: W/L 68) recurrence free at 3/12, 10 patients (4 B/L:6 W/L) were still awaiting their 12/12 cystoscopy, and a further 8 patients had been lost to follow up (B/L 7: W/L 1) (5 died, 1 refused, 2 lost). Recurrence at 12/12 was seen in 10/66 B/L (15%) vs 12/61 (20%) W/L (p=0.50). No adverse reactions attributable to Hexvix were seen.

7. Study Consort



8. Safety Evaluation

No safety issues have been raised in relation to this study.

3 SAEs were reported – Hyponatraemia, unrelated to the Hexvix trial medication.

No SUSARs or SARs reported.

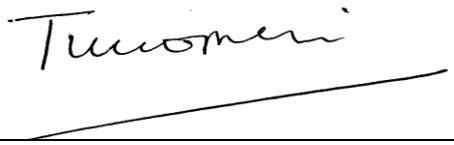
No deaths related to the trial.

9. Conclusions

Although photodynamic diagnosis offers a more accurate diagnostic assessment of a bladder tumour, in this trial we have not shown that this reduces recurrence.

Novel treatment strategies need to be developed to be used in combination with improved diagnostic tools, such as photodynamic diagnosis, if recurrence rates are to be reduced in NMIBC.

10. Declaration

Signature of Chief Investigator:	
Print name:	Mr. T. S O'Brien
Date of submission:	1/06/2012