



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Bilharzial Related Bladder Cancer

A Case Presentation

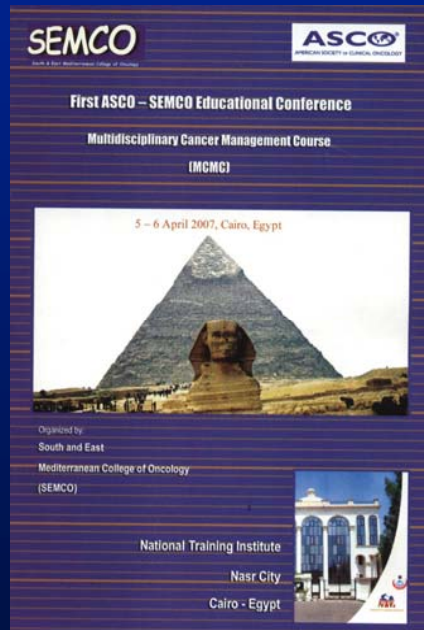
By:

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Case 1

A 66 years old male patient coming from upper Egypt and presented with dysuria, hematuria, and necroturia. PS was 1. On PR examination a T4 bladder mass was discovered. A work up including cystoscopic examination, biopsy from the bladder lesion, CT scan of pelvis and abdomen, X ray chest, bone scan, CBC, liver and kidney function tests were done.

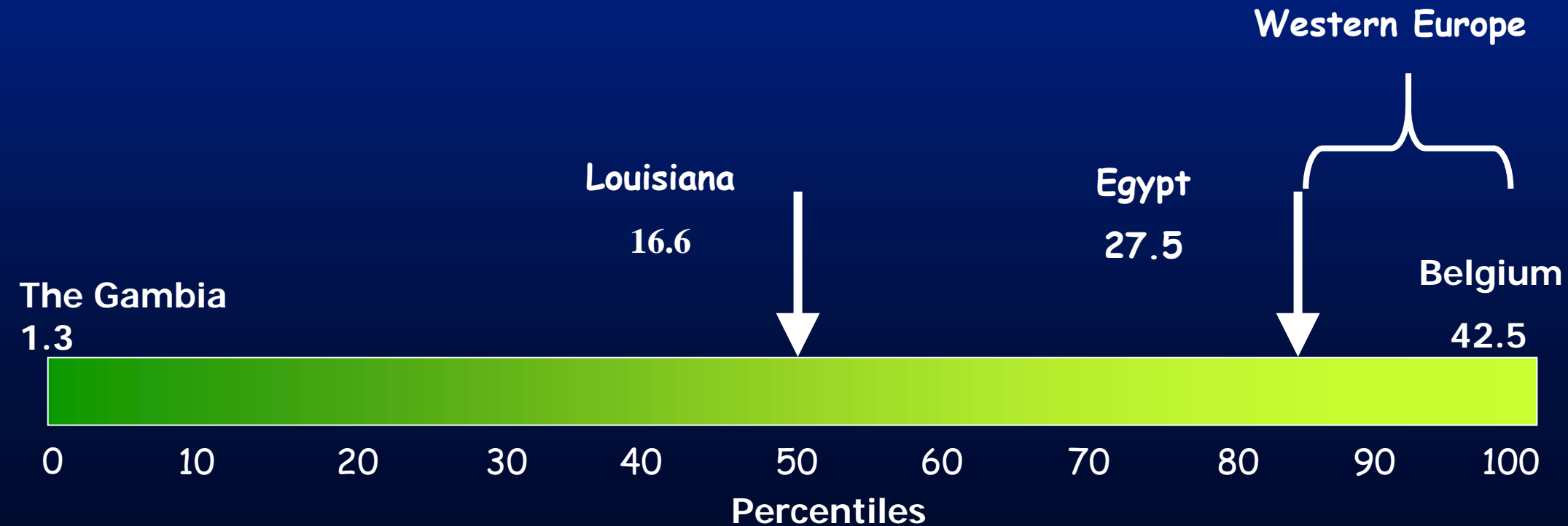
Case 1 (continued)

Final diagnosis was locally advanced inoperable (T4) SCC of the bladder , grade III, with normal kidney and liver functions.

What is the possible further management :

- BSC
- M VAC
- GC
- Other regimens or single agents
- Local radiotherapy

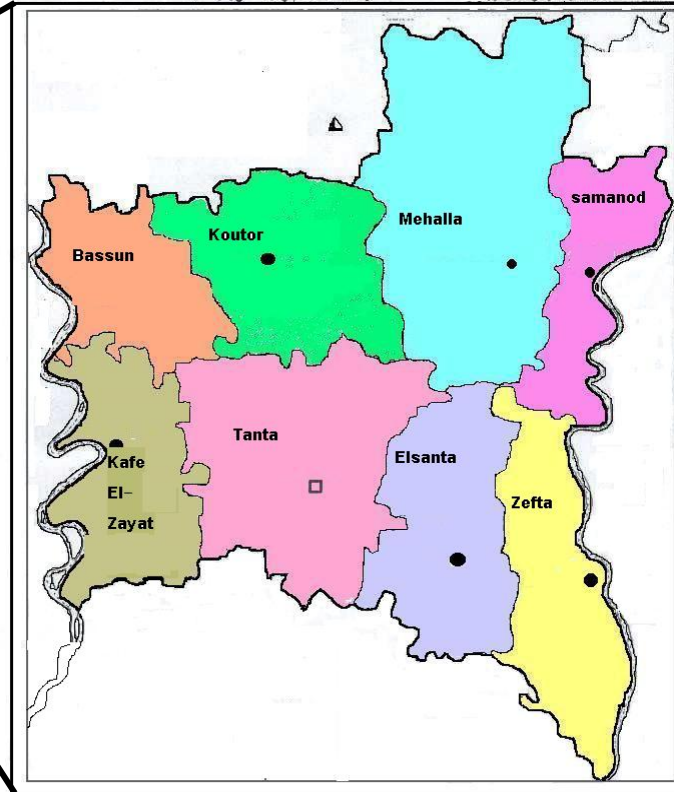
Ranking of ASIR of Bladder Cancer in Egypt relative to worldwide rates (Males)



EGYPT



GHARBIA



Gharbia Population-based registry, 1999 report

5 Most Common sites of cancer Egypt, 1999-2001, Males

	Site	R.F %	ASIR*
1.	Bladder	15.4	26.3
2.	Liver	13.0	21.3
3.	NHL	10.9	15.0
4.	Lung	8.2	14.0
5.	Colon Rectum	3.9	5.6

*ASIR: / 100,000



The National Cancer Institute Cairo University

www.nci.edu.eg

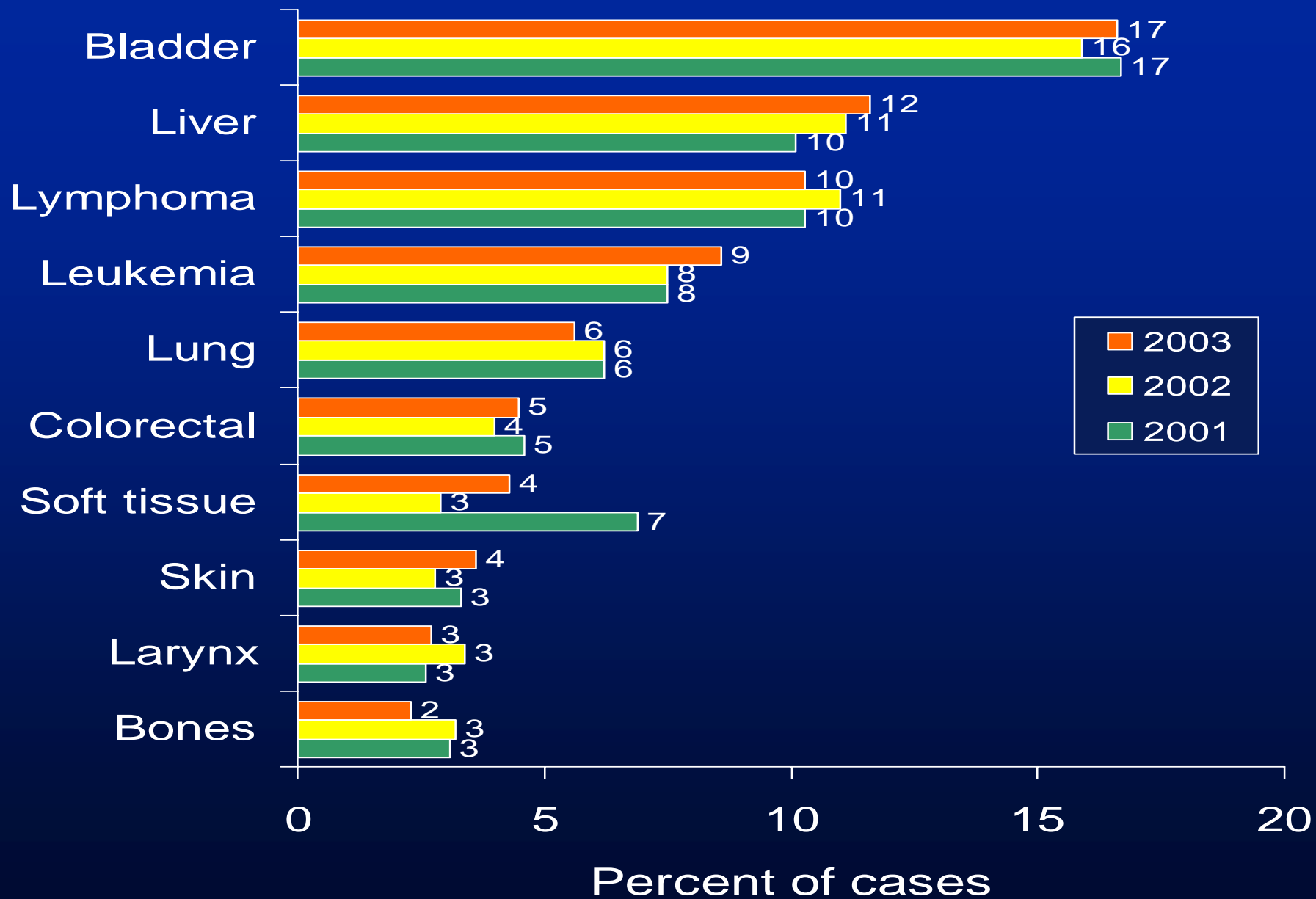


Cairo University

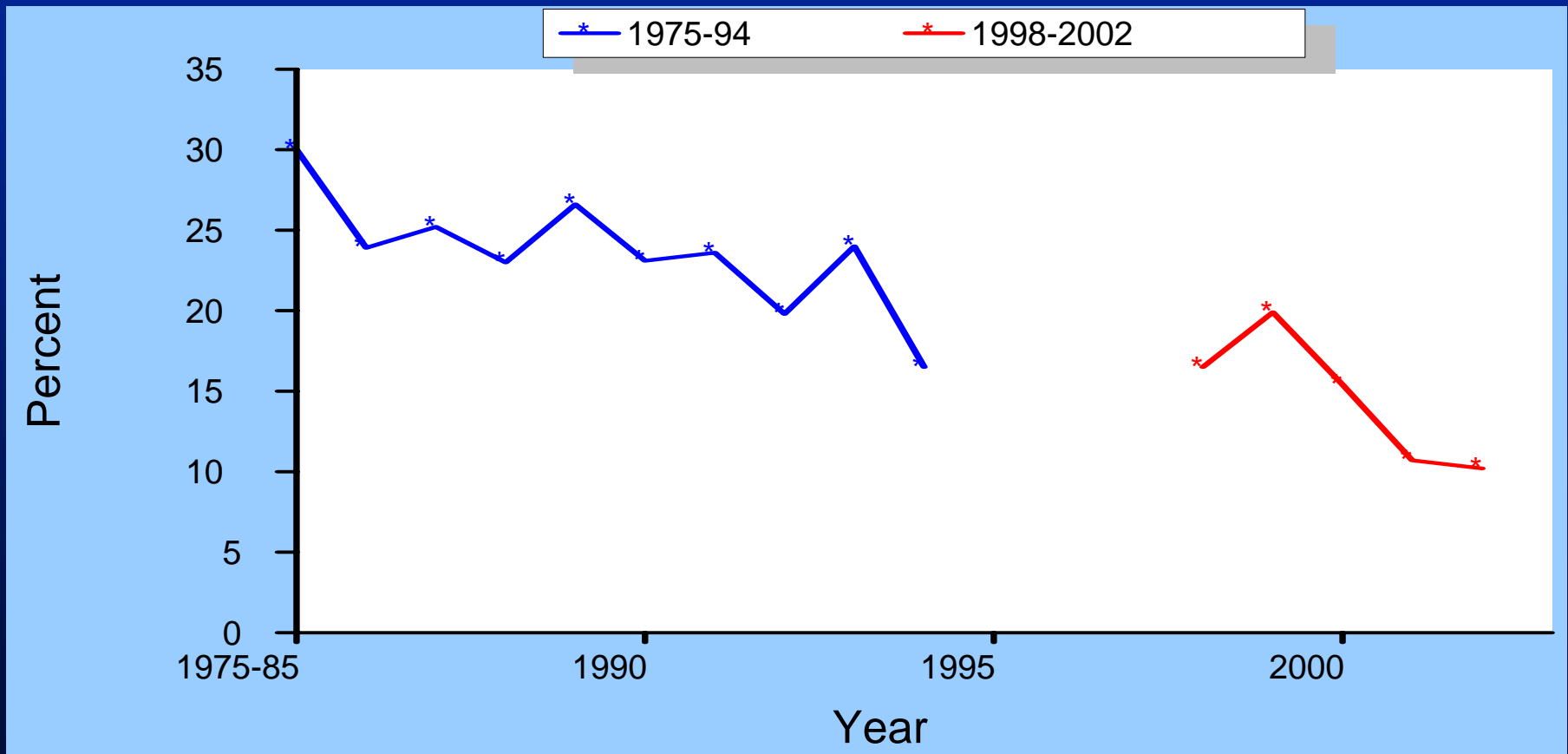


National Cancer Institute

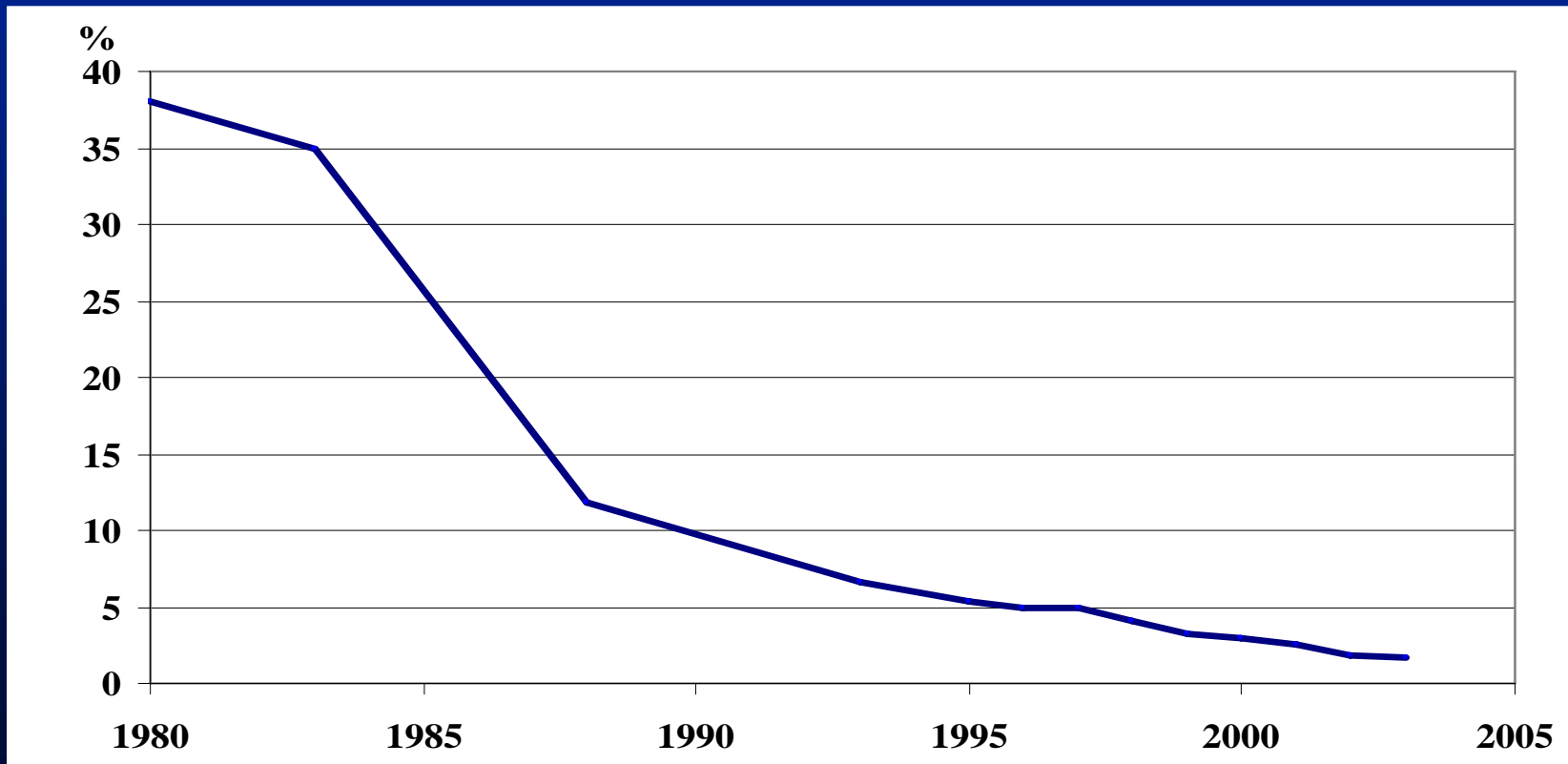
Most Common Sites in Males



Relative Frequency of Bladder Cancer, NCI 1975-2002



Prevalence of schistosomiasis in Egypt: 1935-2003



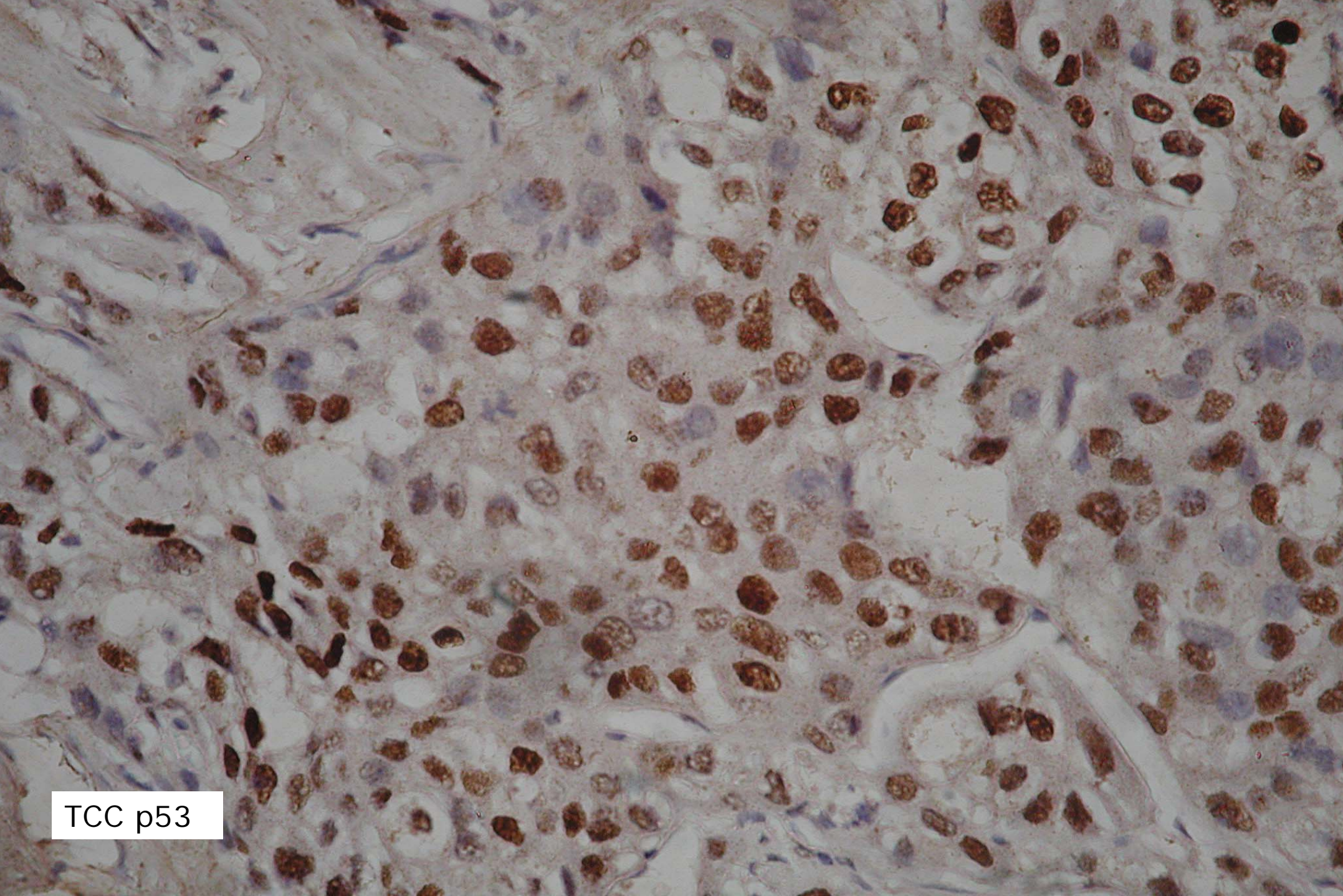
Two Cancer Pathology Registries, NCI
Nadia Mokhtar, Iman Gouda, Iman Adel, 2005

Period	1985-1989	2003-2004
R. freq of bladder ca	26%	14%
Age range	51-60	61-70
M:F	3.7	4.1
Multiple tumors	1.7%	5.8%
Radical cystectomy	80%	36%
Squamous ca	58%	27%
Transitional ca	31%	66%
Late stages III & IV	86%	40%
Bilharzia ova	61%	38%

CANCER GENES

IN BILHARZIA-ASSOCIATED BLADDER CANCER

P53 mutations	33 to 40%
P53 over-expression	20 to 36%
mdm2	59%
High Ki-67 index	72%
ras	14%



TCC p53

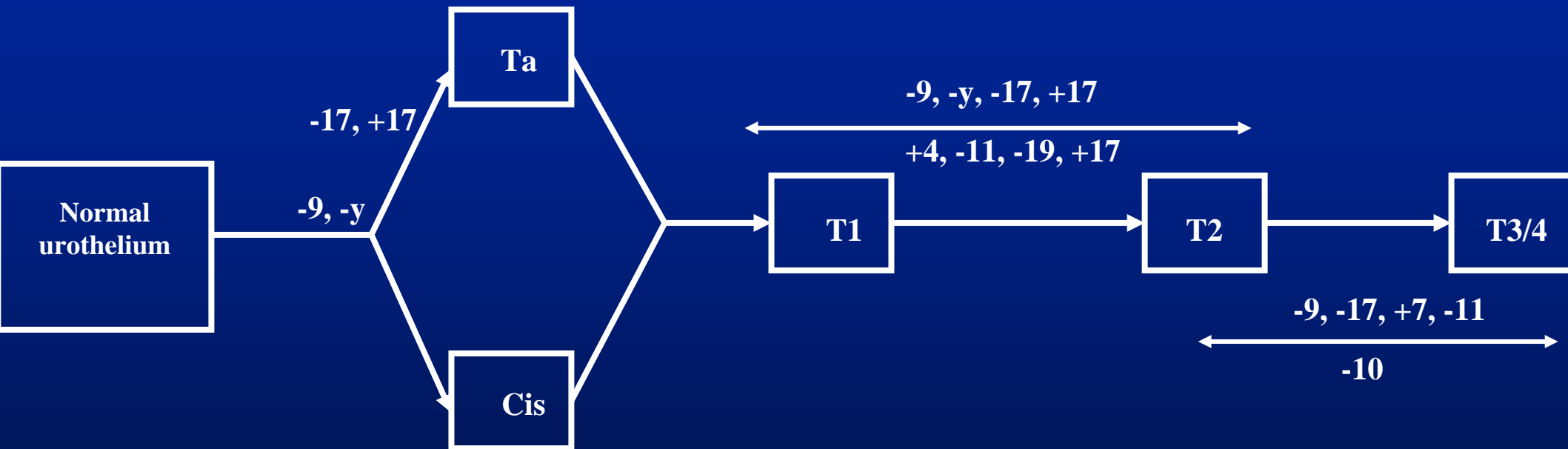
CHROMOSOMAL CHANGES IN BILHARZIA-ASSOCIATED BLADDER CANCER

	Squamous	Transitional
9p deletion	92%	39%
17p deletion	38%	60%
7 aberrations	79%	100%
17 aberrations	29%	84%

NORMAL

PRECANCER

CANCER



PROPOSED SEQUENCE OF CHROMOSOMAL
ABBERATIONS OF BABC

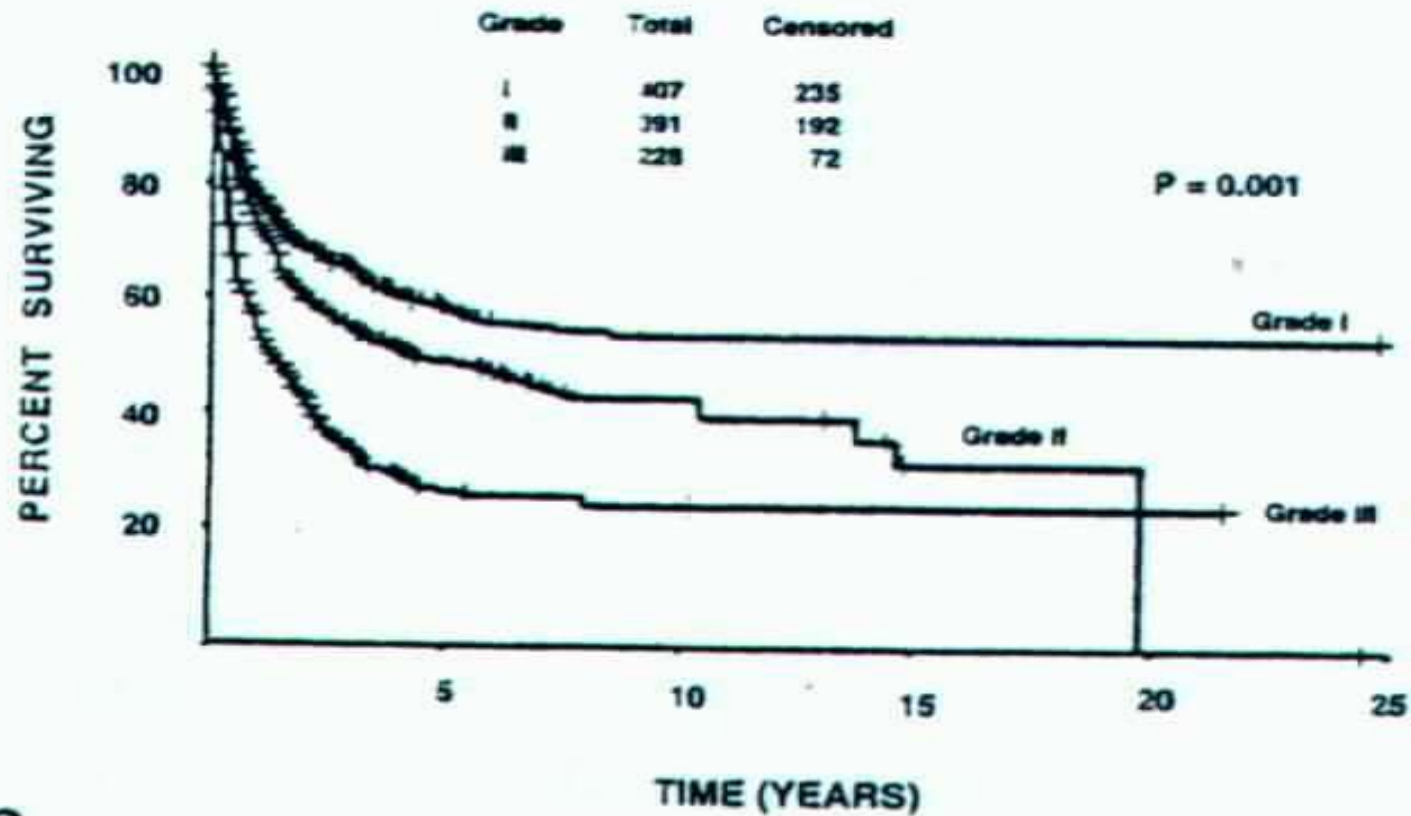
What is the standard treatment of bilharzial related invasive bladder cancer ?

Radical cystectomy is the only curative modality so far available with overall survival rates :

30 % - 45 %

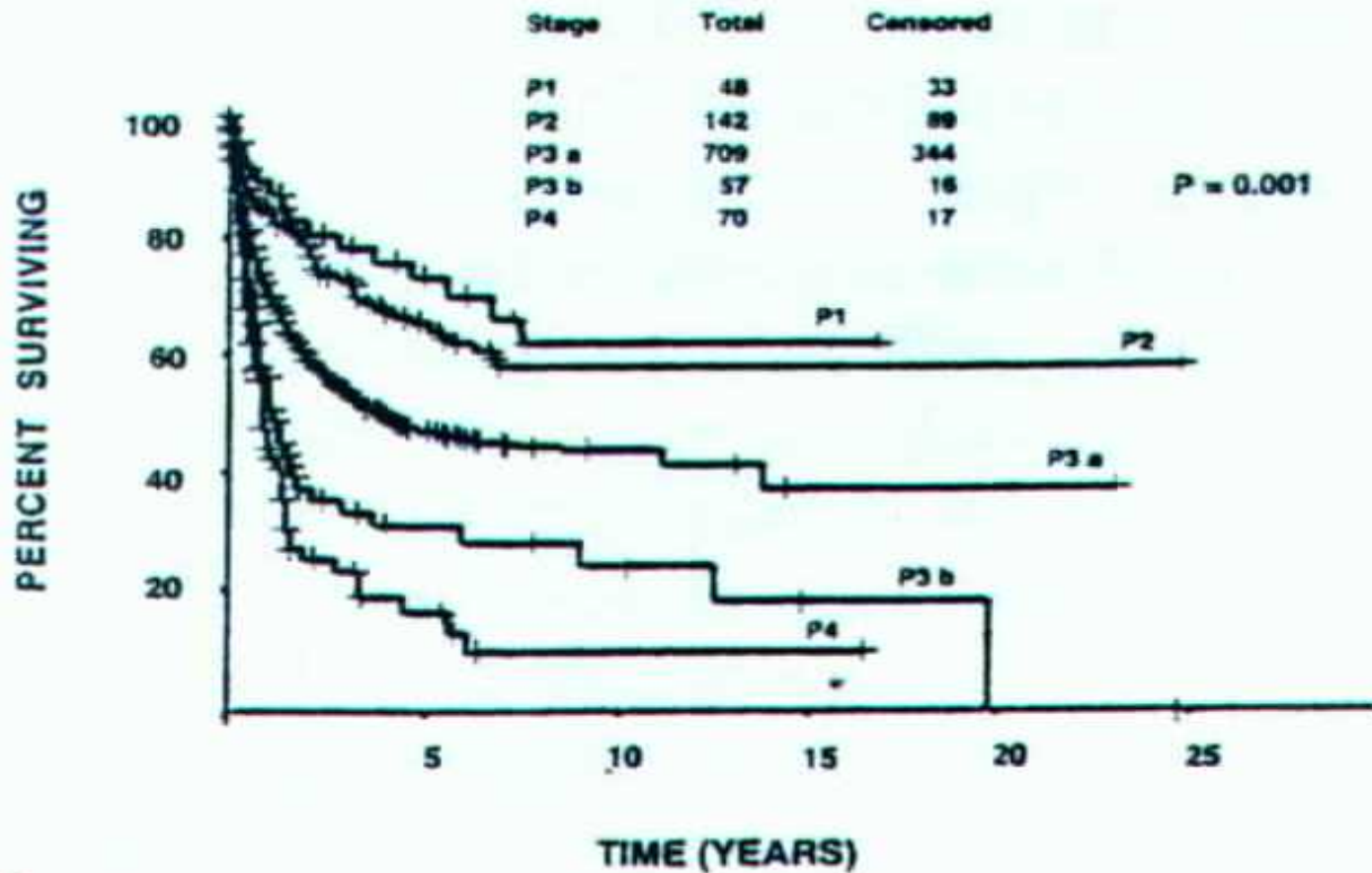
What are the prognostic factors of bilharzial related invasive bladder cancer ?

Survival and Tumor's Grade



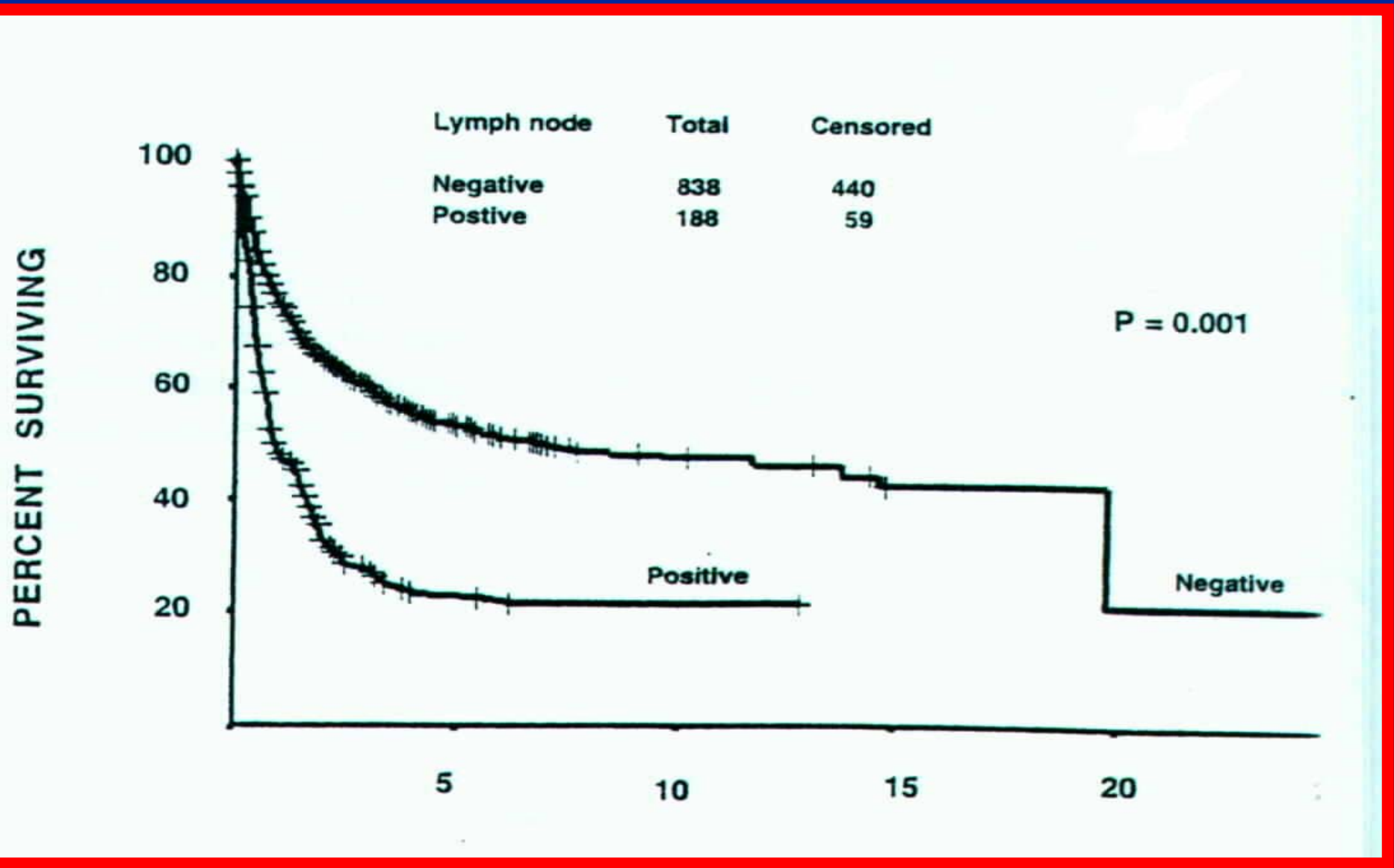
C

Survival and Tumor's Pathologic Stage



A

Survival and Lymph Nodal Status





Urologic Oncology: Seminars and Original Investigations 23 (2005) 254–260

**UROLOGIC
ONCOLOGY**

Original article

A prognostic index (bladder prognostic index) for bilharzial-related invasive bladder cancer

Hussein Khaled, M.D.^{a,*}, Omar El Hattab, M.D.^b, Doaa Abdel Moneim, M.D.^a,
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Three prognostic factors

- T stage
- Grade
- Lymph node status

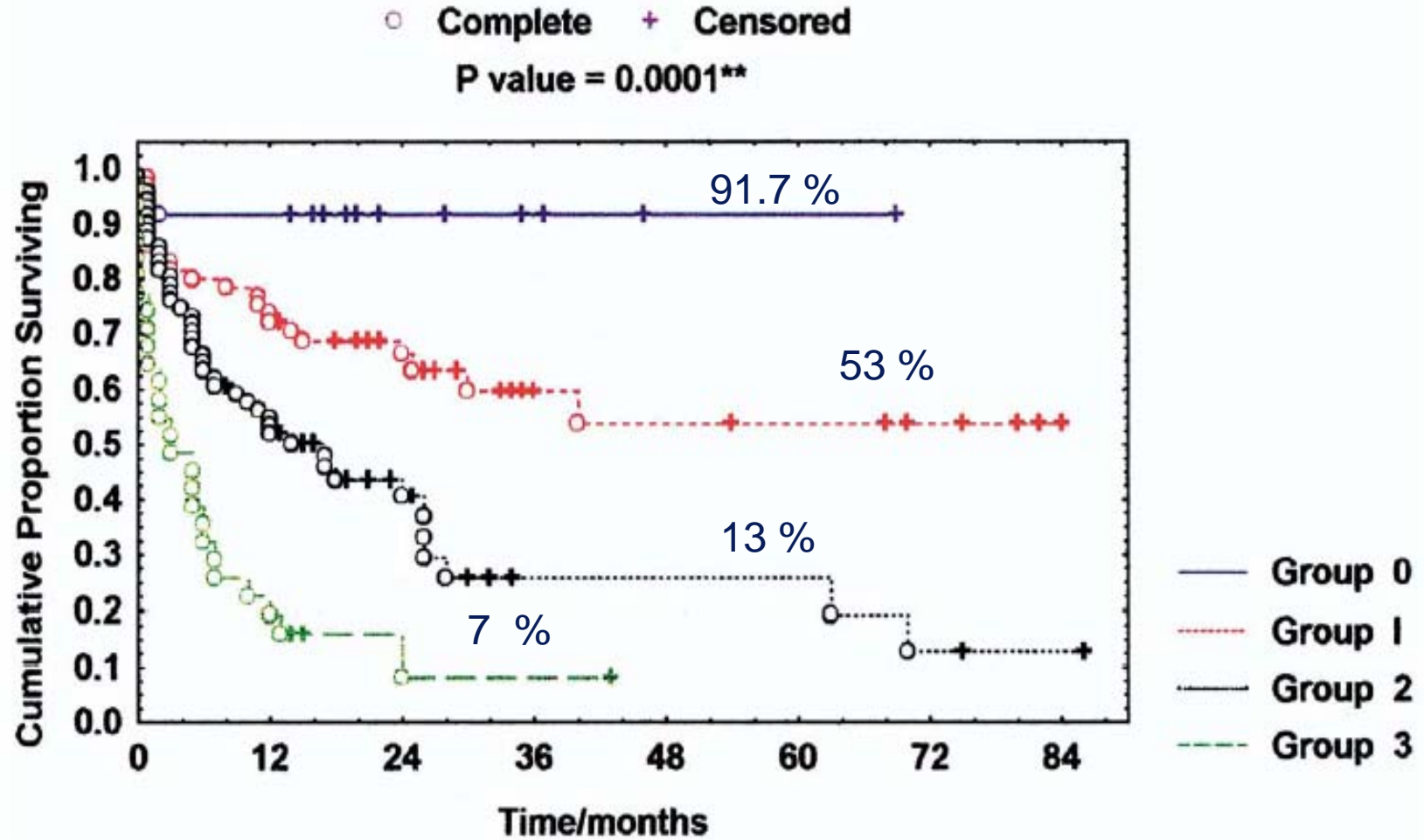


Fig. 2. Disease-free survival in relation to the prognostic group. (Color version of figure is available online.)

The Role of Systemic Therapy in Urinary Bladder Cancer (Bilharzial)

- **Treatment of metastatic disease**
- **Role of adjuvant and neoadjuvant chemotherapy**
- **Role of combined chemo-radiotherapy**

Results of therapy

Drug	No. of patients					
	Evaluable	CR	PR (CR+PR)	Imp.	SD	PD
Bleomycin	21	0	0 (0 %)	2	6	13
Doxorubicin	27	0	0 (0 %)	2	4	21
Tenoposide	26	0	1 (4 %)	2	6	17
5-fluorouracil	32	0	2 (6 %)	3	17	10
Methotrexate	14	0	1 (7 %)	0	2	11
Cisplatin	18	1	2 (16 %)	0	3	12
Dibromodulcitol	22	1	3 (13 %)	0	6	12
Cyclophosphamide	21	1	3 (19 %)	2	9	6
Pentamethylmelamine	25	1	7 (32 %)	2	9	6
Etoposide`	19	0	7 (36 %)	3	5	4
Hexamethylmelamine	26	0	10 (38 %)	12	0	4
Ifosfamide	20	0	8 (40 %)	2	2	8
Vincristine	25	2	9 (44 %)	0	8	6
Vindesine	18	3	10 (41 %)	0	9	10
Epidoxorubicin	18	0	9 (50 %)	0	7	2
	18	0	11 (60 %)	0	7	0

Bilharzial Bladder Cancer Active Single Agents

• Epidoxorubicine	60%
• Vincristine	44%
• Ifosfamide	40%
• Etoposide	36%
• hexamethylmelamine	38%
• Vindesine	46%

Acta Oncol. (89) , 28 , 1 : 73

**Combination Chemotherapy
for
Advanced Bilharzial Bladder
Carcinoma**

Bilharzial Bladder Cancer
Combination Chemotherapy
(EV - IE)

Epidoxorubicin - Vincristine
Alternating with
Etoposide – Ifosfamide

Ann. Oncol. (96) , 7, 751

*Treatment Results
of the 22 Evaluable Bladder Cancer Patients*

• CR	1	(4.5 %)
• PR	8	(36.5 %)
• Improvement	3	(13.6 %)
• S.D.	6	(27.2 %)
• I.D.	4	(18.2 %)
• TOTAL	22	(100 %)

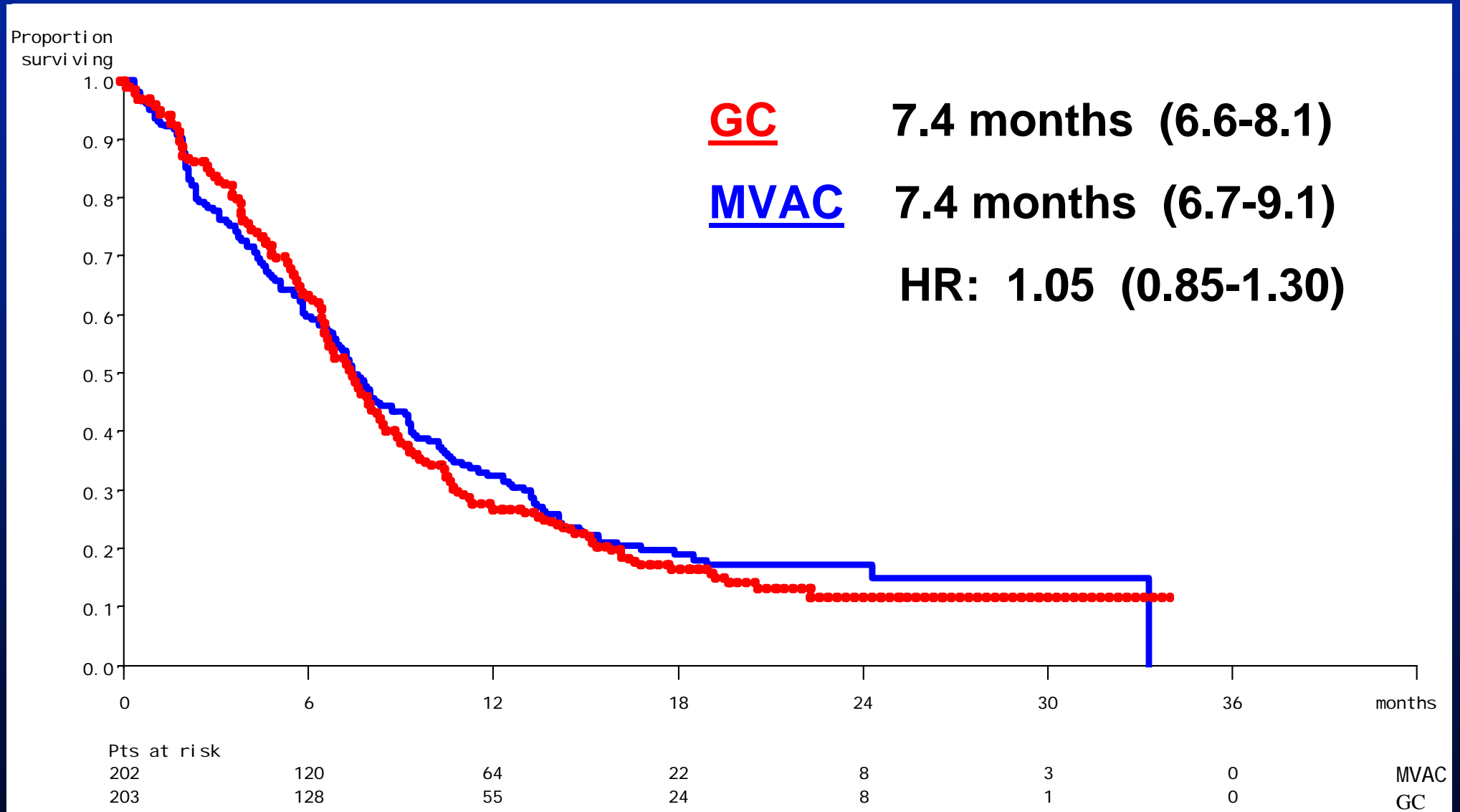
RANDOMIZED PHASE III STUDY IN METASTATIC BLADDER CANCER



Study initiated Nov. 1996 - recruitment completed Sept. 1998

GC versus MVAC

Time to progressive disease



GC versus MVAC

Infections (grade 3-4)	3%	15%
Mucositis (grade 3-4)	1%	22%
Diarrhea (grade 3-4)	3%	8%
Alopecia (grade 3)	11%	55%
Anemia (grade 3-4)	27%	18%
Thrombocytopenia (grade 4)	29%	13%
Neutropenia (grade 4)	30%	65%
Neutropenic fever	2%	14%
Neutropenic sepsis	1%	12%
Toxic deaths	1%	3%

GEMZAR + Cisplatin
in Bilharzial Bladder Cancer
NCI - Cairo

Treatment Schedule

Gemcitabine	1000 mg/m² I.V. days 1,8 & 15
Cisplatin	70 mg/m² I.V. day 2
	Every 28 days

GEMZAR + Cisplatin in Bilharzial Bladder Cancer NCI - Cairo

- Treatment Summary:

- **Evaluable** **33**
-

- Response Rate:

- **CR** **8**
- **PR** **10 (54%)**
- **Improvement** **3**

Responses Include Liver and Lung metastases

GEMZAR + Cisplatin
in Bilharzial Bladder Cancer
NCI - Cairo

- **Response Rate**

	PR	CR
TCC	6	6 (12/20 , 60%)
SCC	4	2 (6/12 , 50%)
- **Median Response Duration**
5 + months (1 - 22+ months)
- **Median Observation Time**
7.5 + months (2 - 24+ months)

*Gemcitabine plus Cisplatin is an active combination for
Bilharzial related bladder cancer
(Response rate 54 %), with a moderate toxicity profile*

European J. Cancer (2000) , 36: s34-s37

Other Trials

- **Gem (low dose – prolonged infusion) +
Cisplatin**

Treatment Schedule

Gemcitabine	250 mg/m²	over 6 hours infusion
		days 1, and 8
Cisplatin	70 mg/m²	day 2

Every 21 days

RESULTS

- Treatment Summary

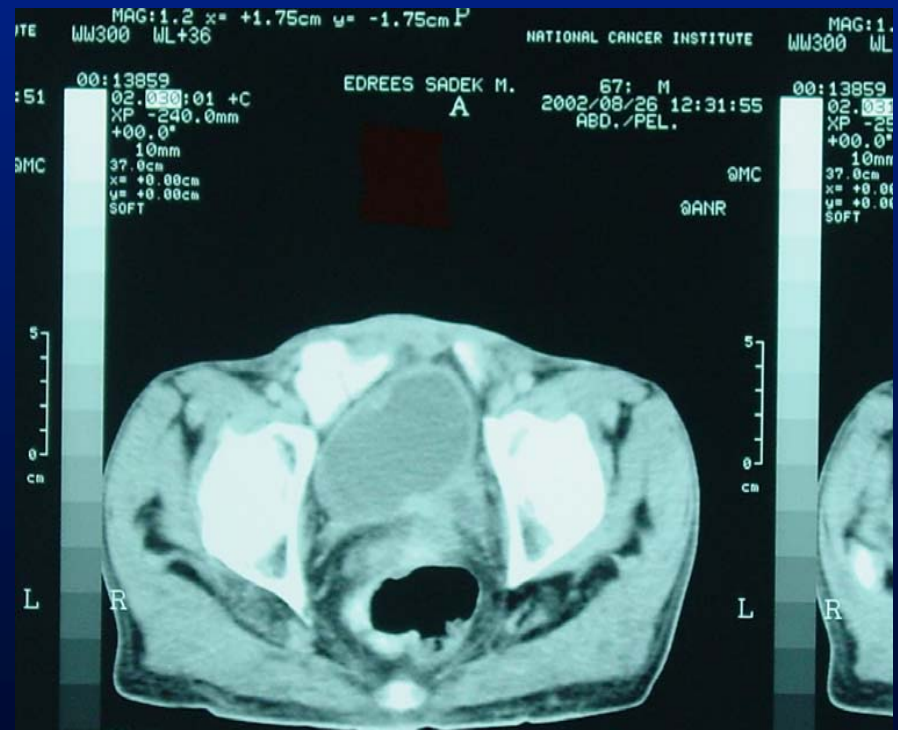
Evaluable patients	55	
Total cycle number	240	
Median cycle number	4	(range:1–6 cycles)
- Response Rate

CR	5	(9 %)
PR	23	(42%)
Minor response	4	(7 %)

Responses were observed in all disease sites

Case 1 (management)

This patient has received a combination of low dose GC.



The Role of Systemic Therapy in Urinary Bladder Cancer (Bilharzial)

- **Treatment of metastatic disease**
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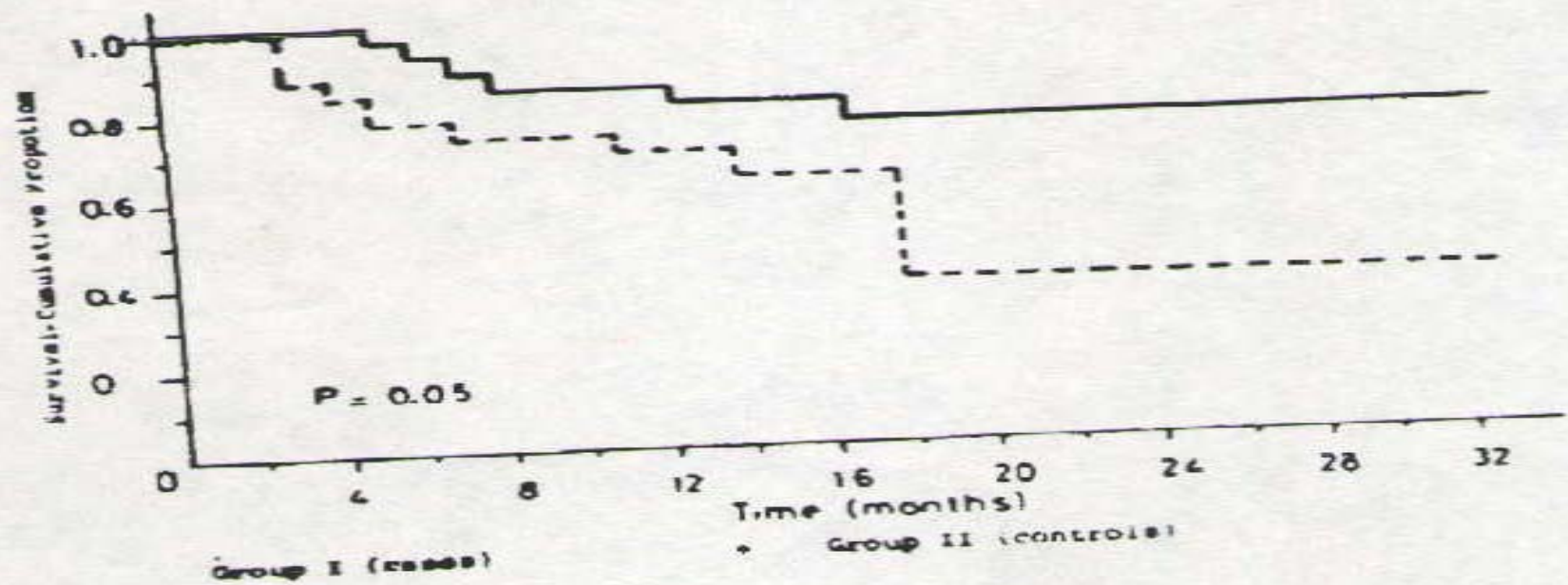
Original article

A randomized pilot study of high-dose epirubicin as neoadjuvant chemotherapy in the treatment of cancer of the bilharzial bladder

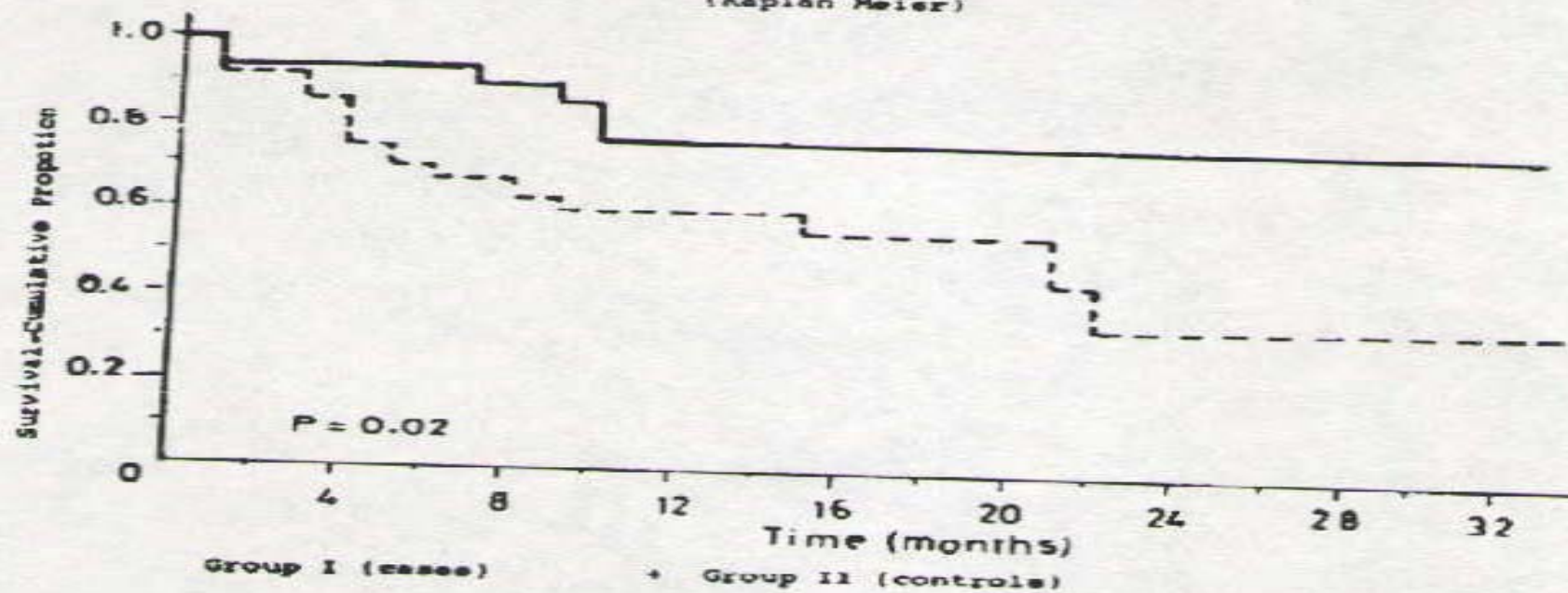
N. Gad El Mawla,¹ M. A. Mansour,¹ S. Eissa,¹ N. M. Ali,¹ I. Elattar,¹ M. R. Hamza,¹
H. Khaled,¹ N. Habboubi,² I. Magrath³ & I. Elsebai¹

¹National Cancer Institute (NCI), Cairo, Egypt; ²Farmitalia Carlo Erba, Italy; ³National Cancer Institute, Bethesda, Maryland, USA

DISEASE FREE RATE (Kaplan Meier)



SURVIVAL RATE (Kaplan Meier)



RANDOMIZATION

Surgery alone 107

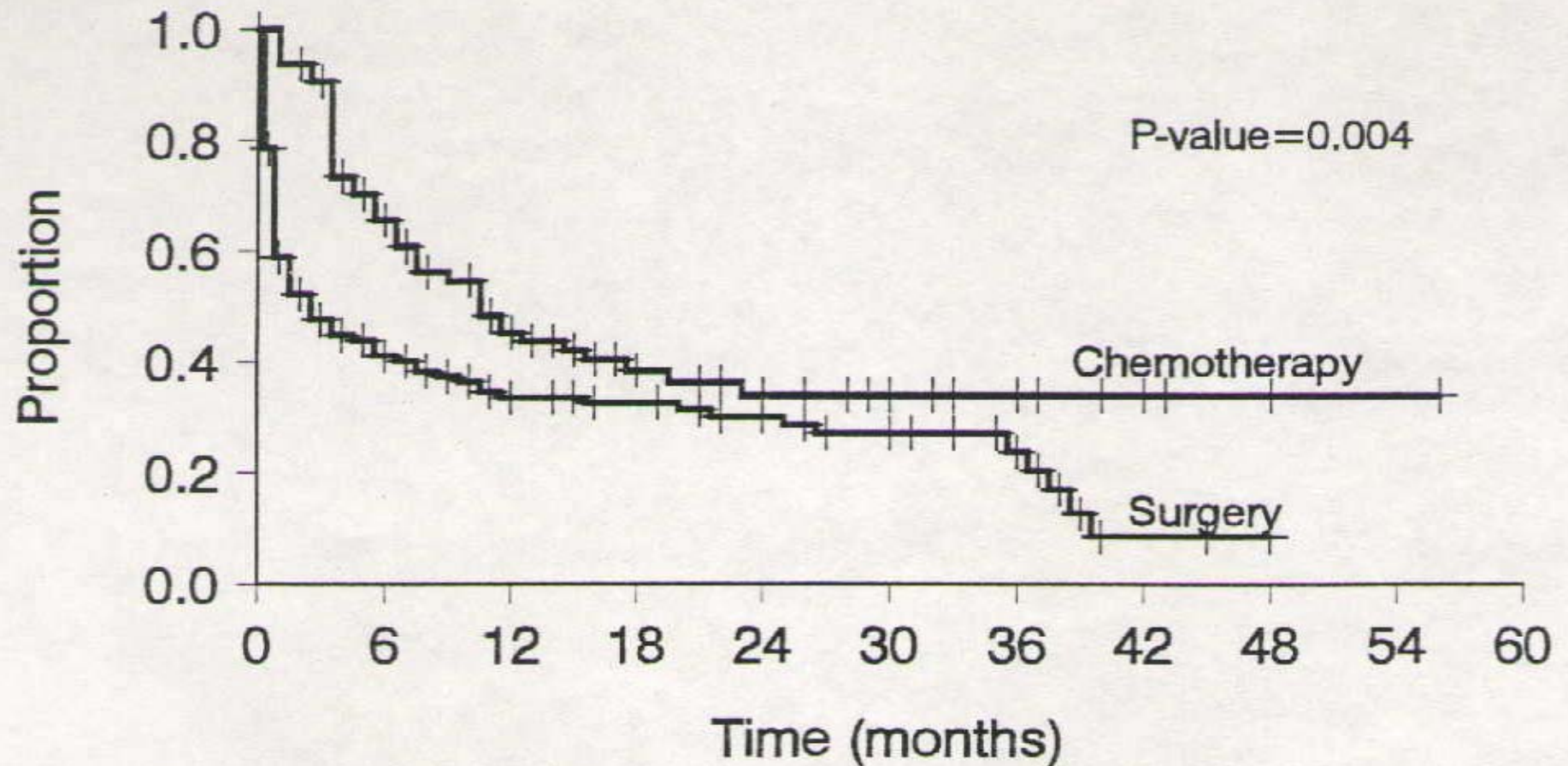
Surgery + 64

chemotherapy

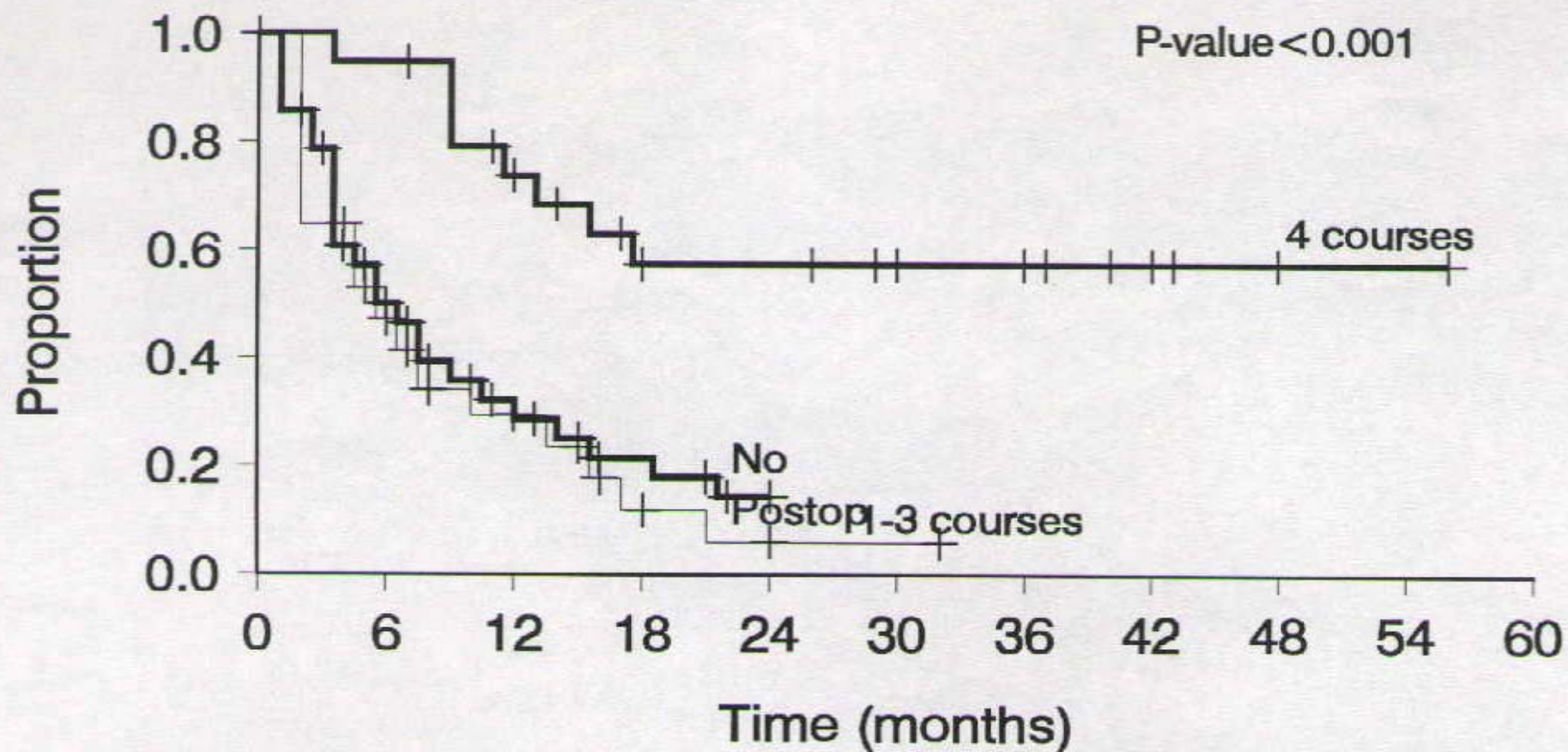
CHEMOTHERAPY GROUP

Pre-op.	Surgery	Post-op.	No
2	+	0	28
2	+	1	9
2	+	2	3
2	+	3	5
2	+	4	19
<hr/>			64

Overall Survival for Bladder Cancer Cases by Treatment.



Overall Survival for Bladder Cancer Cases by Number of Post Operative Chemotherapy Courses.



Bilharzial Bladder Cancer

Drug Therapy

Invasive Tumors

Superficial Tumors

Advanced, metastatic, and recurrent

Invasive operable

Little experience

Single agent phase II trials

1975

now

Neoadjuvant

Pilot study

Phase III trial

CT-RT

Combination Chemotherapy

phase II trials

Epi VCR - Ifo VP16

Gemz – DDP (2)

Phase III trial

(combination vs single agent)

Adjuvant

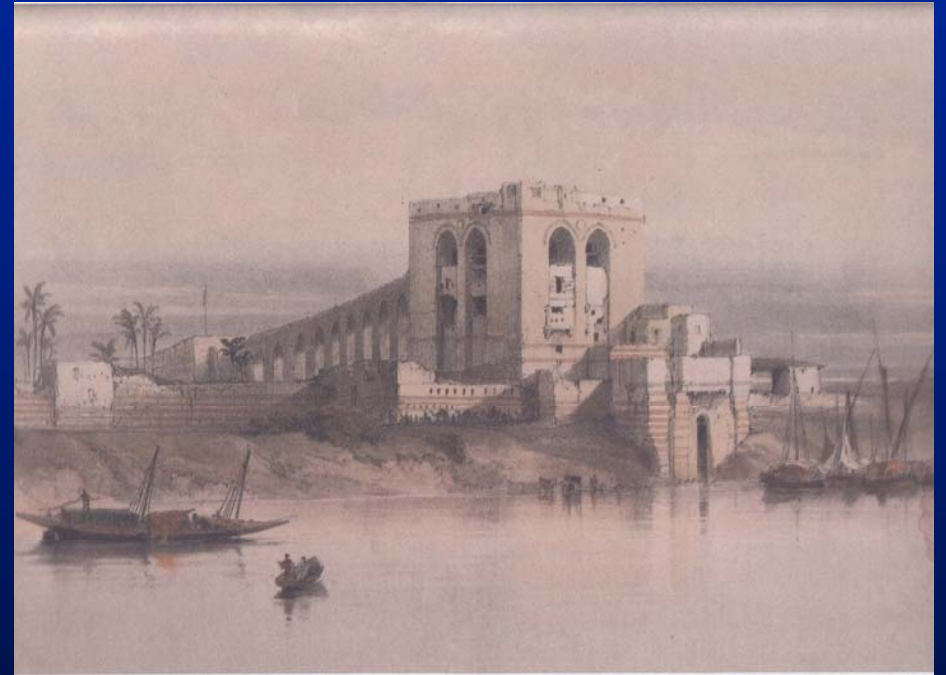
Classic surgery

Modified surgery

Tumor Repository:

- **Bladder tumor tissue touch print**
frozen
paraffin block
- **Bladder Bilharzial tissue**
- **Bladder Normal Tissue**
- **Patients' Serum**
- **Patients' Urine**
- **Patients' Lymphocytes**
(So far: 500 Cases)

National Cancer Institute Cairo University



Thank you