

**QUALITÀ E QUANTITÀ DI VITA
NEL PAZIENTE
CON NEOPLASIA VESCICALE T1 HG (G3)**

**Trattamento conservativo Vs
cistectomia precoce**

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I TERMINI DEL PROBLEMA...


PROGNOSI DEI T1 G3 con o senza CIS

NMIBC ALTO GRADO	Modalità di presentazione	Recidiva 5 anni %	Progressione 5 anni %
T1G3	T1G3 Monofocale 1° d	46	17
	T1G3 plurifocale 1° d	62	17
	T1G3 recidivo monof	62	17
	T1G3 recidivo plurif	62	45
T1G3 + CIS	Monofocale 1 diagnosi	46	45
	Plurifocale 1 diagnosi	62	45
	Monofocale recidivo	62	45
	Plurifocale recidivo	62	45

EORTC RISK TABLES FOR STAGE Ta and T1 BLADDER CANCER

T1G3

I TERMINI DEL PROBLEMA...

- Progressione e sopravvivenza malattia specifica diventano gli obiettivi primari di efficacia
 - Sia le linee guida AUA [Hall 2007] che Europee [Babjuk M, 2008] dichiarano che il BCG con mantenimento (i.e. per almeno 1 anno) è la terapia raccomandata per questo tipo di patologia
 - Questo implica superiorità del BCG alla sola TUR, alla chemioterapia e (almeno) non inferiorità alla cistectomia
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TUR+BCG E' MEGLIO DELLA TUR da sola?

POCHI STUDI e RETROSPETTIVI!

Author	N of patients	Main outcome	Comment
Patard JJ, 2002 Retrospective, case-control	TUR alone (N=30) TUR+BCG (N=50)	Median follow up 63 months Progression and CSS 22% and 90% with BCG vs 46.7% and 70% with TUR alone respectively	TUR+BCG may improve survival over TUR alone
Shahin O, 2003 Retrospective, case-control	TUR alone (N=92) TUR+BCG (N=61)	<ul style="list-style-type: none">- Median follow-up 5.3 ys- Recurrence: 70% BCG vs 75% TUR alone- Progression: 33% BCG vs 36% with TUR- TTP: 38 mo with BCG vs 28 mo without BCG- CSS: 77% BCG, 79% without BCG	BCG delays recurrence and progression. No influence on overall and CSS

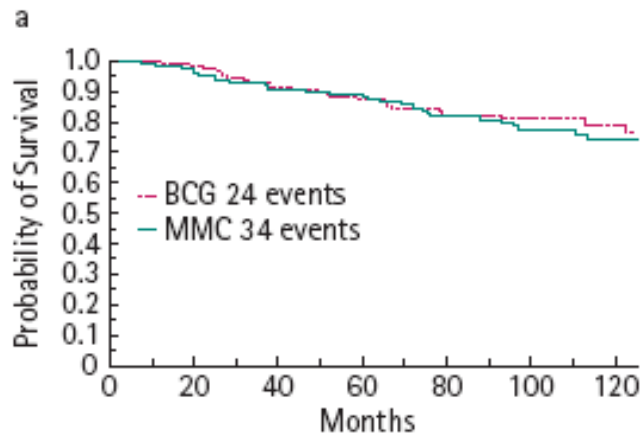
TUR+BCG meglio di TUR+chemioterapia (MMC)?

Author	Type of "high risk" patient	End points	N of patients	Main outcome	Comment
Gardmark T, 2007 RCT	Ta G1-3 or T1 G1-2 multi recurrent or any T1G3 and CIS	Progression (increased in stage from Ta to T1 and from T1 to T2), CSS	130 BCG 2 ys maint 131 MMC 2 ys maint	Median follow up survivors: 123 months Progression 23% with MMC and 19% with BCG	No significant difference in progression, overall survival and CSS between BCG and MMC
Hall MC, 2007 (AUA Guidelines panel) Meta-analysis of RCT	No G1 tumours or any T1 or any CIS	Progression	MMC maint (N=79) BCG induct (N=260) BCG maint (N=341)	Recurrence : 62% MMC maint, 32% BCG induct, 34% BCG maint. Progression : 10% MMC maint, 14% BCG induct, 14% BCG maint	BCG better on recurrence, no significant difference in progression

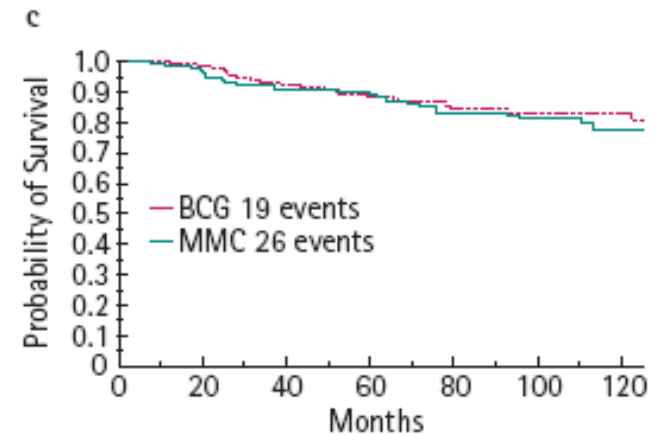
MMC vs BCG nei NMIBC ad ALTO RISCHIO

Sopravvivenza e progressione dopo 10 anni

progressione



Sopravvivenza CS



- RCT, 261 pazienti, FU mediano 123 mesi
- BCG (Danish strain)
- progressione 34 MMC vs 24 BCG (p=0.26)

Gardmark et al, BJU Int 2007

TUR+BCG meglio di TUR+chemioterapia (MMC)?

CIS primitivo, secondario, concomitante

Author	N of patients	Main outcome	Comment
<p>Sylvester RJ, 2005</p> <p>Meta-analysis of 9 RCT studies</p>	<p>345 BCG (75% maint)</p> <p>355 chemotherapy (50% MMC, 95% maint)</p>	<p>Median follow up: 3.6 ys</p> <p>OR=0.53 (p=0.0002) for CR and 0.47 (p=0.008) for recurrence in favour of BCG</p> <p>OR=0.74 (p=0.2) favouring BCG for progression</p>	<p>BCG significantly better than chemotherapy for CR and recurrence. Superiority over MMC significant only when maintenance BCG used.</p> <p>Insufficient power to state superiority of BCG in progression and survival</p>

IL BCG (+ CISTECTOMIA TARDIVA) E' EQUIVALENTE ALLA CISTECTOMIA PRECOCE?

SOLO STUDI RETROSPETTIVI

- **NESSUNA DIFFERENZA**

(Thalmann et al J Urol 2004)

N=29 EARLY CYSTECTOMY vs N=92 TURB+BCG

- **A FAVORE DELLA CISTECTOMIA**

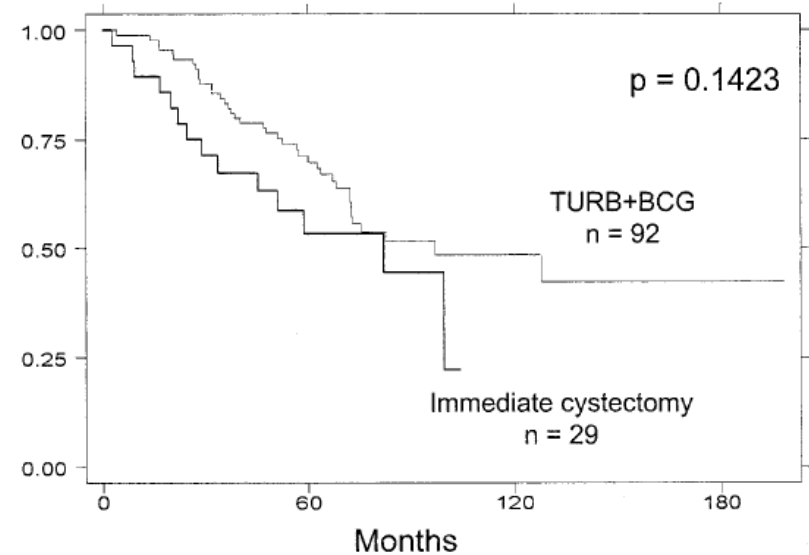
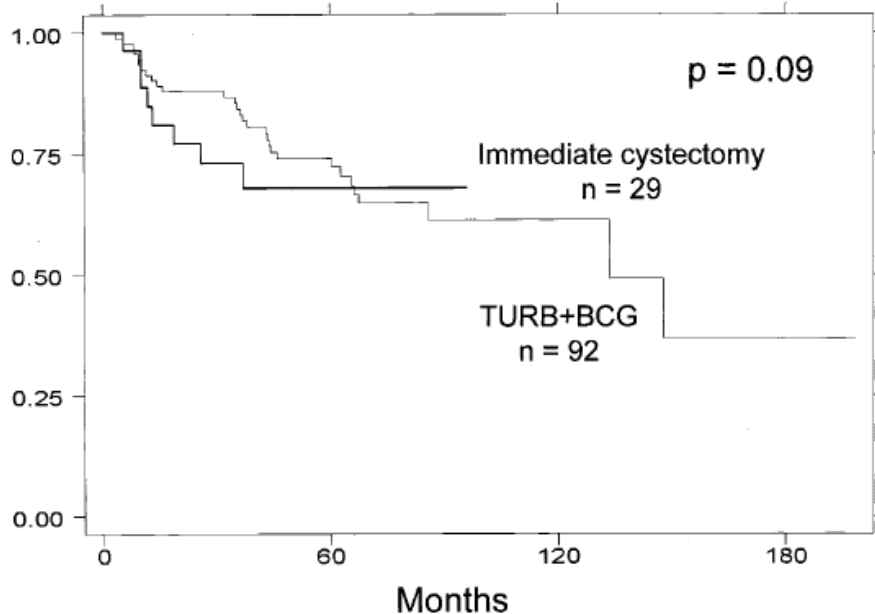
(Denzinger S, Eur urol 2008)

- N=101, 51% cistectomia precoce, 49% cistectomia tardiva
 - Selezionati per > 2 fattori di rischio associati al T1G3
 - CSS a 10 anni: 78% cistectomia precoce vs 51% tardiva
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PRIMARY T1G3 BLADDER CANCER: ORGAN PRESERVING APPROACH OR IMMEDIATE CYSTECTOMY?

GEORGE N. THALMANN,* REGULA MARKWALDER, OSAMA SHAHIN,† FIONA C. BURKHARD,
WERNER W. HOCHREITER AND URS E. STUDER

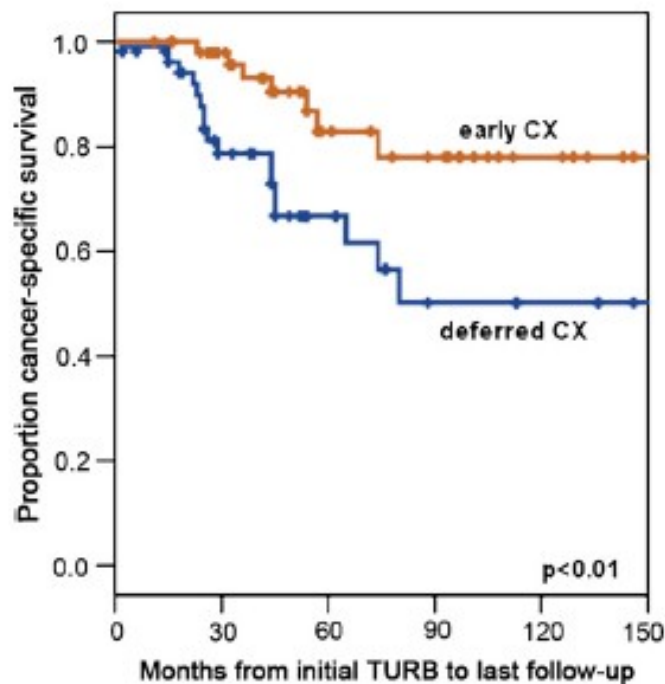
progressione



sopravvivenza

Early Versus Deferred Cystectomy for Initial High-Risk pT1G3 Urothelial Carcinoma of the Bladder: Do Risk Factors Define Feasibility of Bladder-Sparing Approach?

Stefan Denzinger*, Hans-Martin Fritsche, Wolfgang Otto, Andreas Blana, Wolf-Ferdinand Wieland, Maximilian Burger



Pazienti con ≥ 2 fattori di rischio:

- CIS
- multifocalità
- diametro > 3 cm

Fig. 1 - Kaplan-Meier analysis of cancer-specific survival in patients with early (orange line) versus deferred (blue line) cystectomy.

Il cuore del problema: IL BCG PREVIENE LA PROGRESSIONE DEI NMIBC?

Author	Main outcome	Comment
Sylvester RJ, J Urol 2002 Meta-analysis of 24RCT comparing BCG to either TUR alone or chemotherapy or immunotherapy Ta and T1 (N=3967), CIS (N=896)	Median follow up 2.5 years Progression rate 9.8% with BCG and 13.8% in the control group (27% reduction in the odd of progression with BCG) OR=0.63 favouring BCG when BCG administered with maintenance OR=1.28 (no difference with control group) when BCG administered without maintenance	Overall, BCG reduces the risk of progression when maintenance is used. No significant difference between BCG and MMC
Sylvester R, in press Individual patient data meta-analysis of 7 RCT Intermediate and high risk NMIBC	Overall progression rate 12%, overall mortality 24%	No significant difference in progression and survival rate between BCG and MMC

TERAPIA dei T1G3

CONCLUSIONI

- L'assunto che il BCG sia gold standard nei NMIBC ad alto rischio ha un livello di evidenza elevato solo per il CIS ma molto basso per i T1G3
- BCG “forse” funziona meglio di MMC per la recidiva ma non per la progressione nei T1G3: è sufficiente?
- Le evidenze attuali dimostrerebbero che BCG non previene la progressione nei NMIBC a rischio intermedio...
- Se dobbiamo utilizzare una terapia conservativa nei T1G3 (senza CIS) non vi sono evidenze che BCG sia superiore a MMC