Ongoing Clinical Research with Immune Checkpoint Inhibitors in UBC

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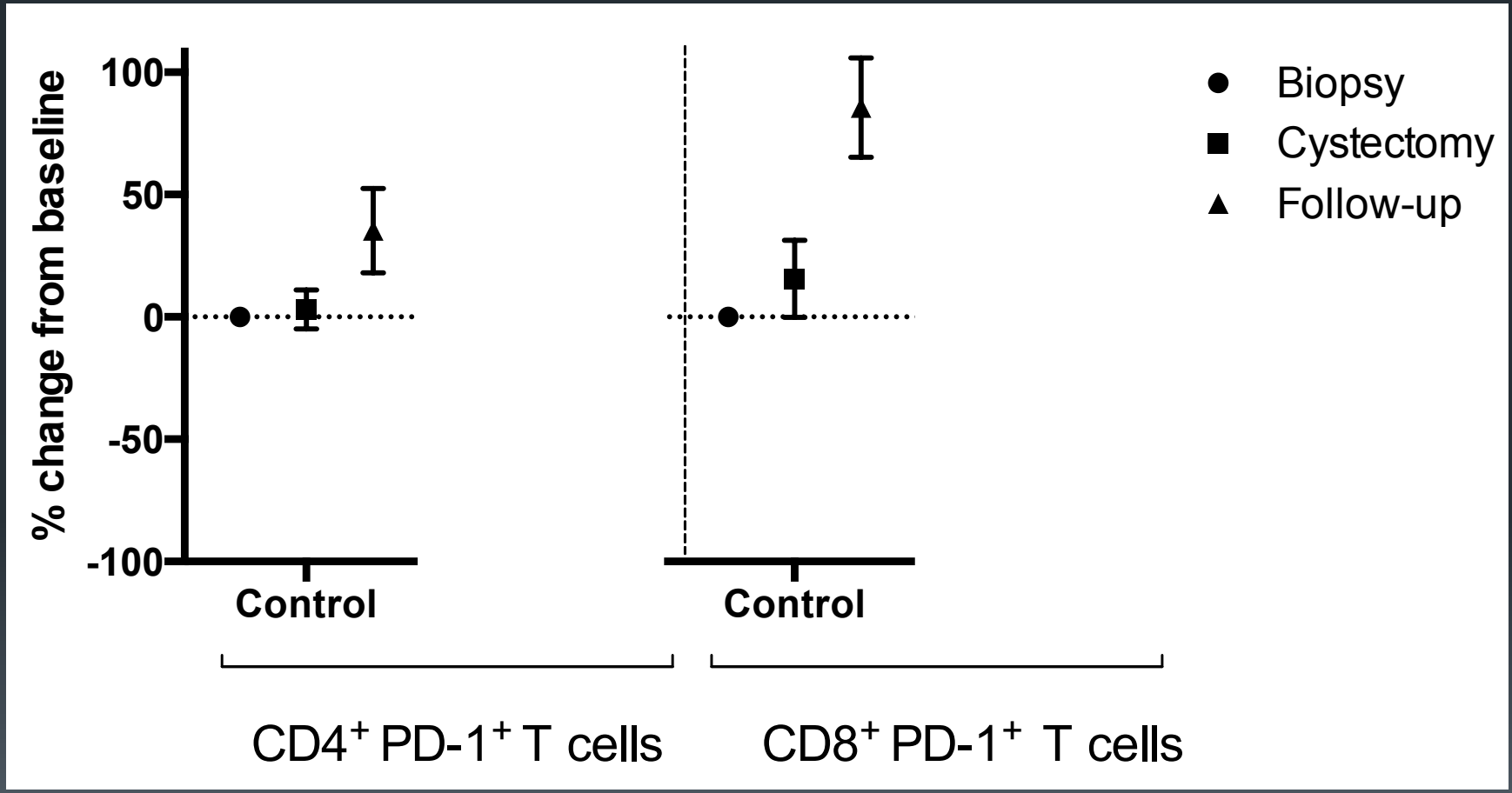
Disclosures

Consulting Agreement	Rapamycin Holdings
Contracted Research	FKD Therapies, JBL Drug Laboratories

Immune checkpoint inhibition with cystectomy: perioperative trial examples

- Pembro neoadjuvant trial
  - T2-T4a N0 urothelial bladder carcinoma (UBC) with residual disease after transurethral resection of the bladder (TURB, surgical opinion, cystoscopy or radiological presence) will receive 3 cycles of pembrolizumab at the dose of 200 mg every 3 weeks prior to surgery
- IMvigor010 – adjuvant atezolizumab (anti-PD-L1) versus observation for high-risk muscle-invasive urothelial cancer after cystectomy

Surgical stress induced immune dysfunction



Svatek, et al. (manuscript in prep)

Rationale, design, entry criteria for trials in non-muscle-invasive bladder cancer (NMIBC)

Risk Stratification in NMIBC

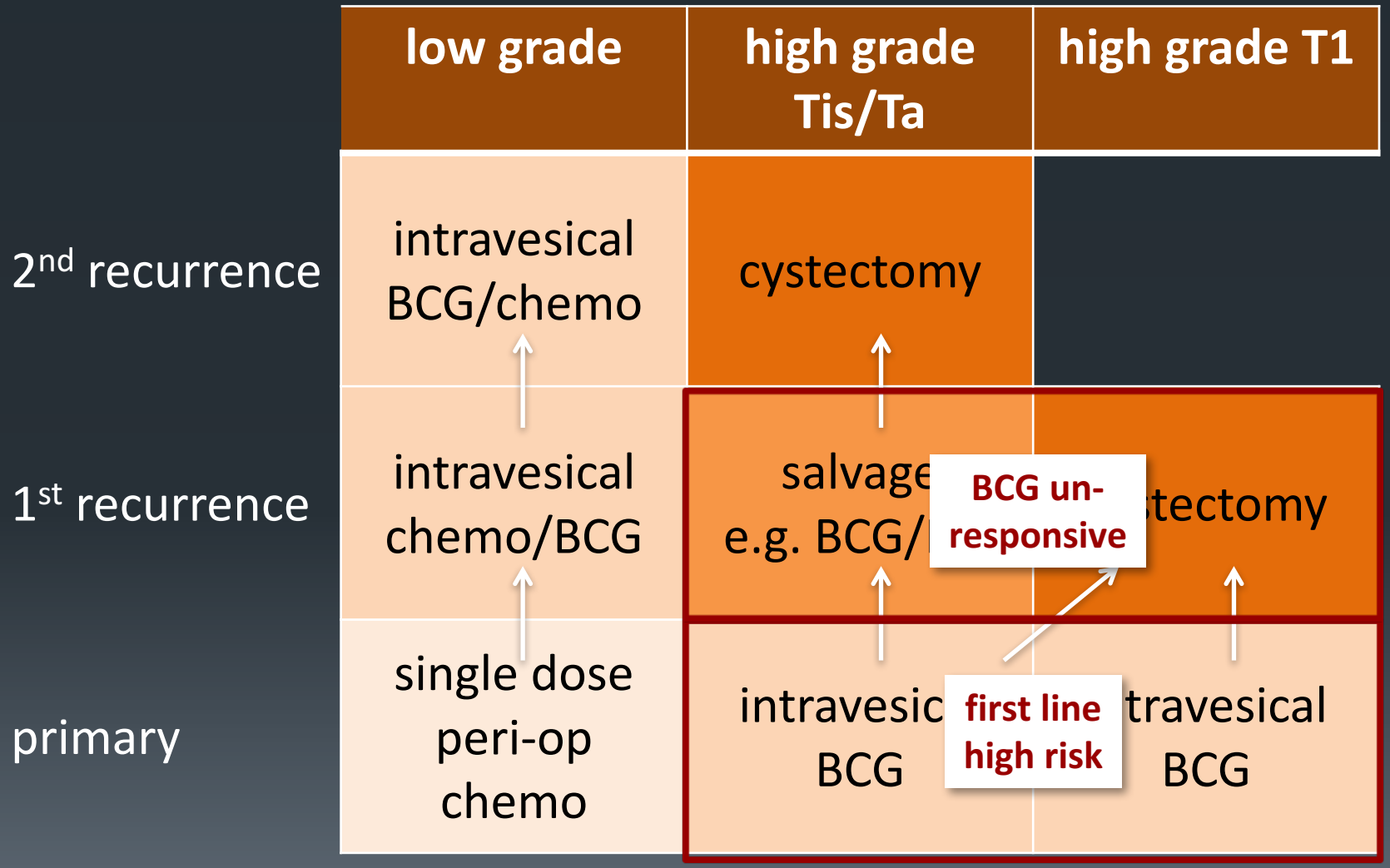
LOW RISK	INTERMEDIATE RISK	HIGH RISK
single low grade ≤3cm incl. PNLMP (50%)	recurrent LG <1 yr >3cm LG multifocal LG low grade T1 high grade Ta ≤3cm	high grade T1 recurrent HG Ta CIS HG after BCG variant histology presence LVI HG in prostatic urethra

AUA Guidelines 2016

Risk-Adapted Intravesical Therapy

- Low risk: single dose peri-operative chemo
- Intermediate risk: adjuvant intravesical chemotherapy or BCG
  - additional intravesical therapy with recurrence
- High risk: intravesical BCG
  - radical cystectomy is standard of care for high grade recurrence after adequate BCG

NMIBC – Disease States



Courtesy of Peter Black

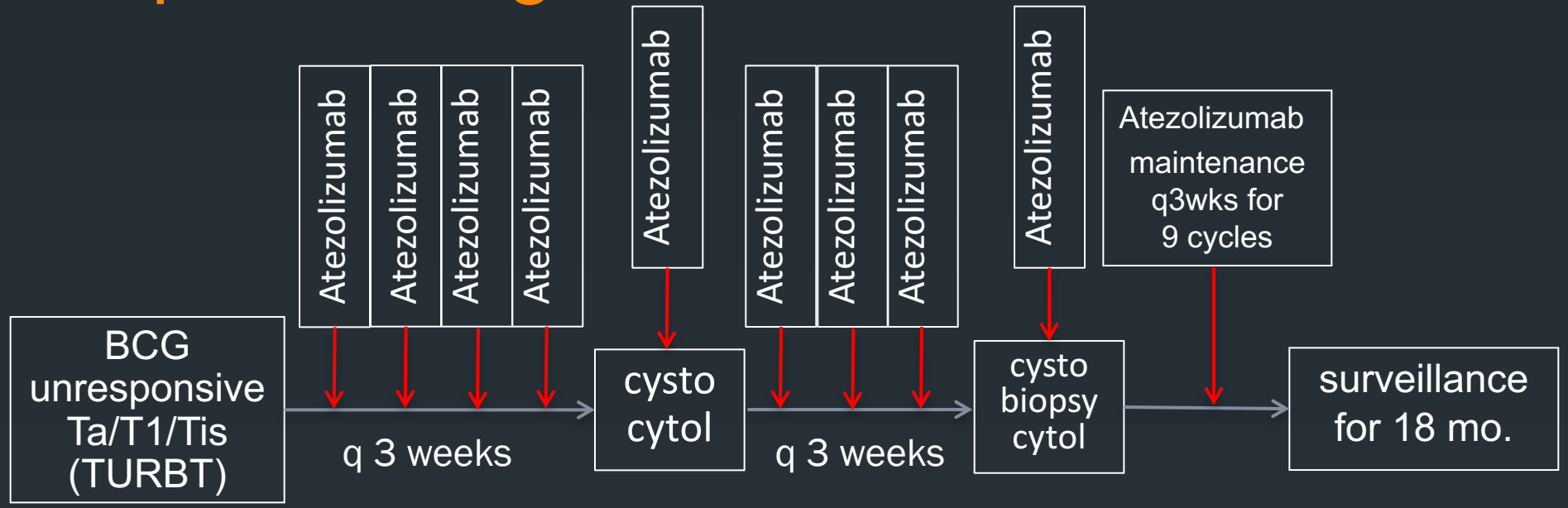
“BCG unresponsive NMIBC”

- Any high grade recurrence after induction + 1st round maintenance, or 2 rounds induction
  - ***Exception***: high grade T1 disease at 3 months (after induction BCG only) is considered “unresponsive”
- For patients who achieve complete response on induction/maintenance BCG: any high grade recurrence within 6 months of last dose of BCG
- Recurrent low grade Ta disease is not considered unresponsive in this context

Novel Immunotherapy NMIBC

- Enhanced BCG
- Vaccines
- Viruses
- Immune checkpoint inhibitors

S1605: Phase II trial of Atezolizumab in BCG-unresponsive high risk NMIBC



13 weeks*

CR @ 25 weeks*
(=6 months post TURBT)

RFS @ 18 months

- registration within 6 weeks of TURBT
- start therapy within 5 days of registration

* time is relative to first dose of atezolizumab

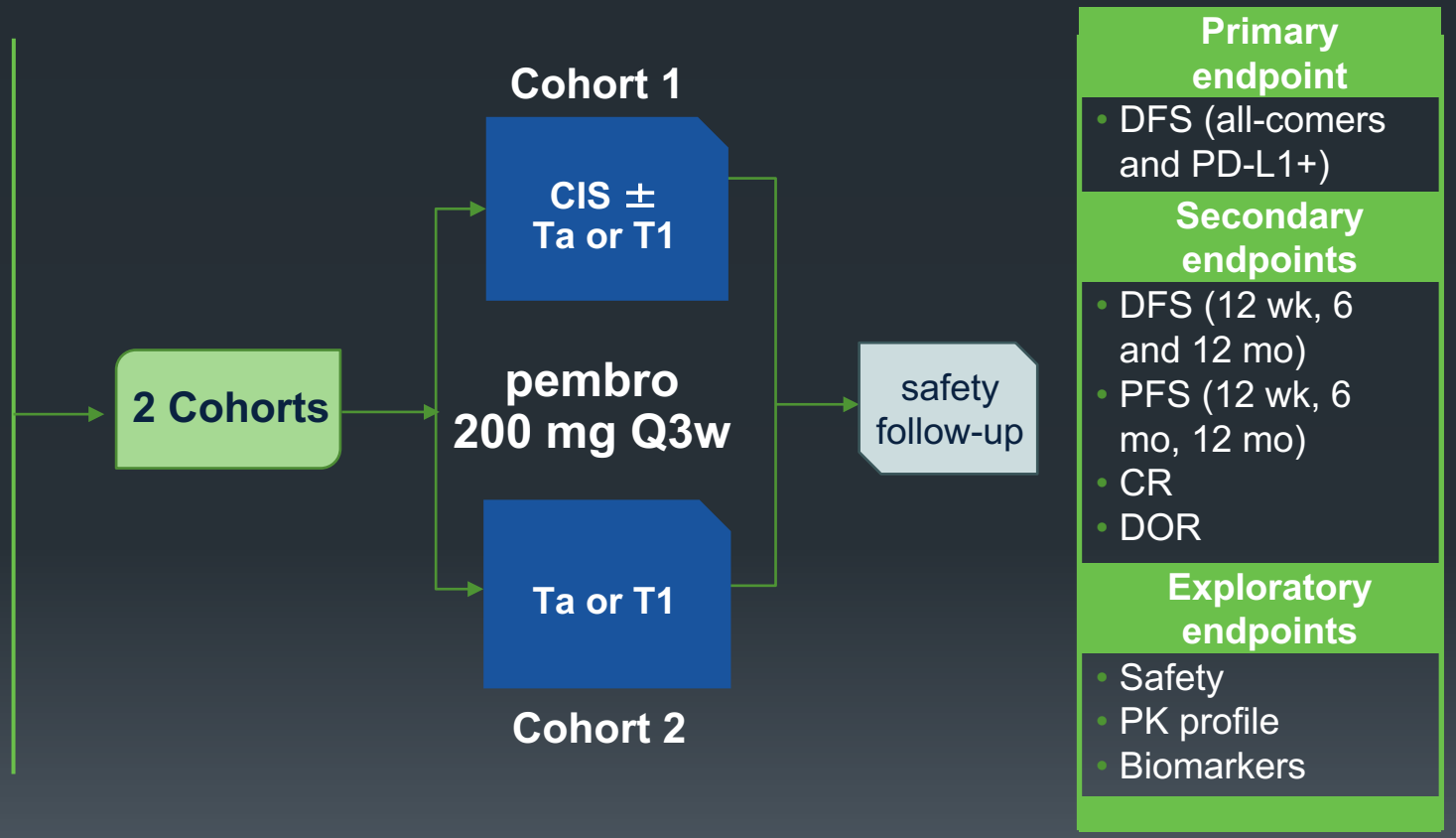
PI: Black & Singh (Lerner)
ECOG/ACRIN: T Bivalacqua
Alliance: M Woods
CCTG: W Kassouf

SWOG Leading cancer research. Together.

KEYNOTE-057: Phase II trial of Pembrolizumab in BCG unresponsive high risk NMIBC

Eligibility

- high risk NMIBC (T1, HGTa, CIS)
- urothelial or mixed histology
- BCG-unresponsive
- ECOG status 0, 1, or 2
- Hemoglobin >9 g/dL

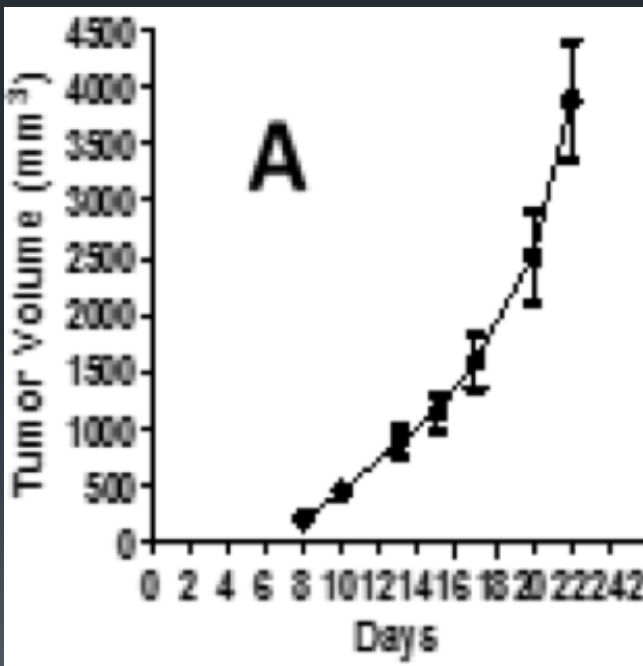


Target enrollment: 260

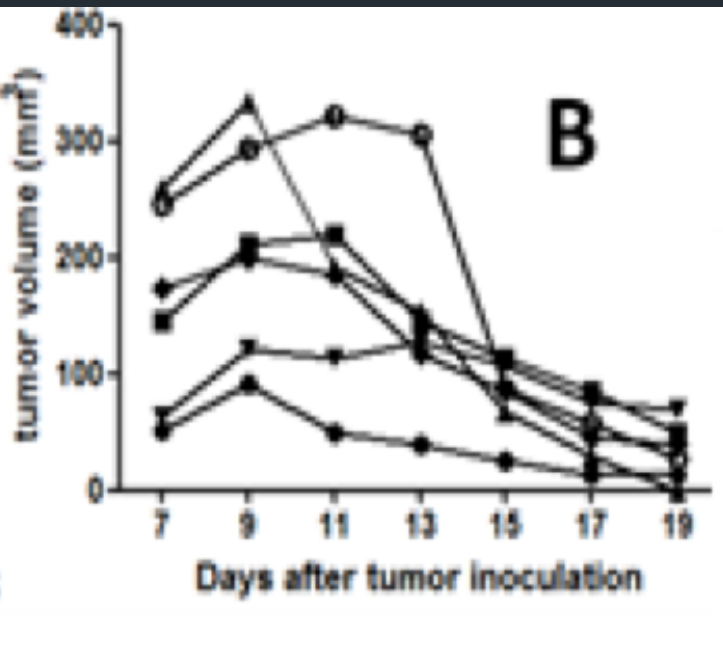
Tumor PD-L1 effects in bladder are distinct

Subcutaneous

MB49 parental



MB49 PD-L1 KO



Bladder