# Immunotherapy in Genitourinary Cancers

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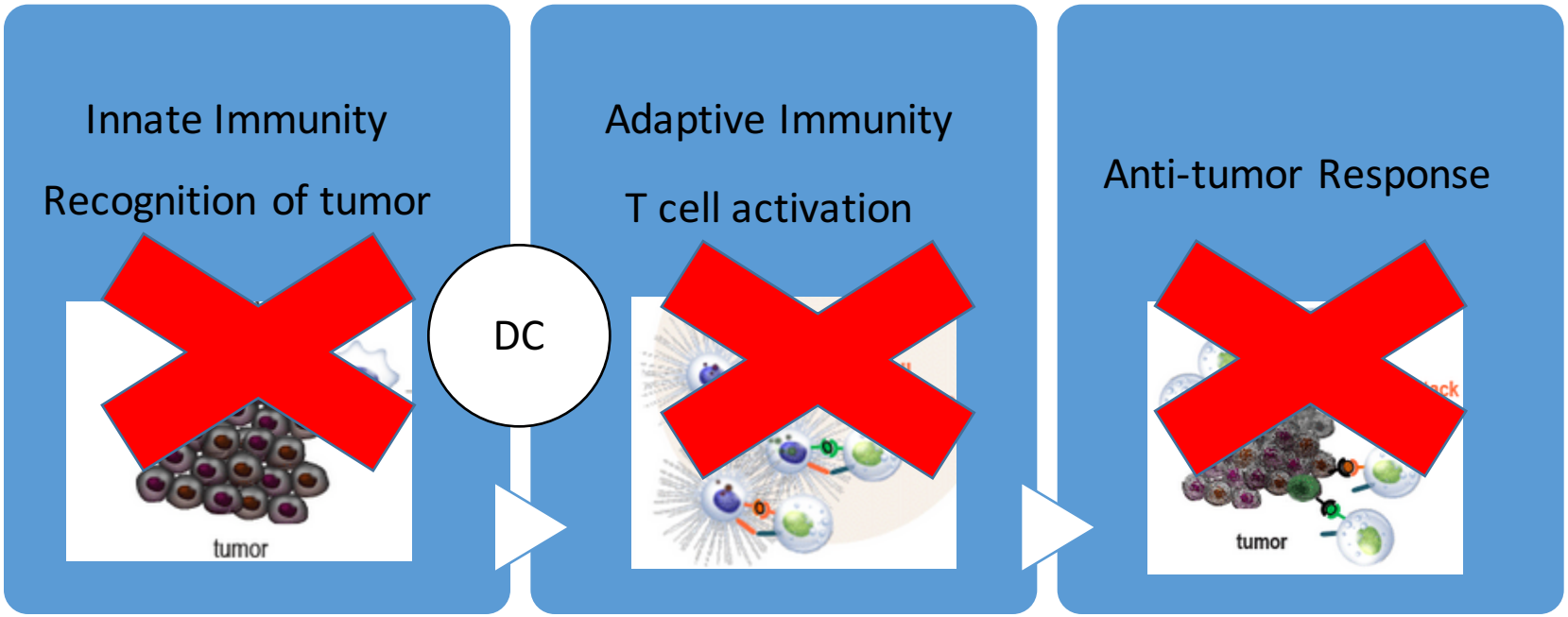
# Outline

- Cancer Immunology
- Current Data of Immunotherapy in GU Cancers
- New Immunotherapy Concepts in GU cancers
- Future Research Directions

# Immune System and Cancer

## Tolerance



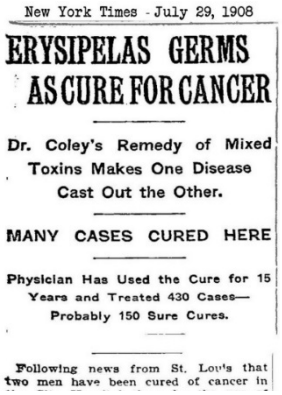

**Defective antigen presentation**

**Inhibition of CTL**

**Immunosuppressive TME**

# Cancer Immunotherapy

## Break tolerance and reinvigorate antitumor immunity


New York Times - July 29, 1908

ERYSIPELAS GERMS AS CURE FOR CANCER

Dr. Coley's Remedy of Mixed Toxins Makes One Disease Cast Out the Other.

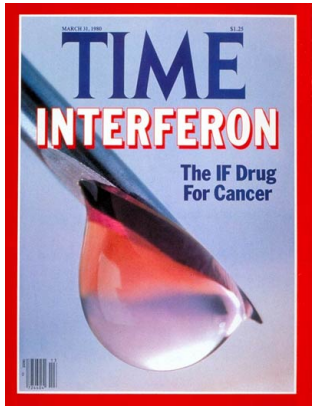
MANY CASES CURED HERE

Physician Has Used the Cure for 15 Years and Treated 430 Cases—Probably 150 Sure Cures.

Following news from St. Louis that two men have been cured of cancer in


Albert Calmette
(1863-1933)


Camille Guerin
(1872-1961)

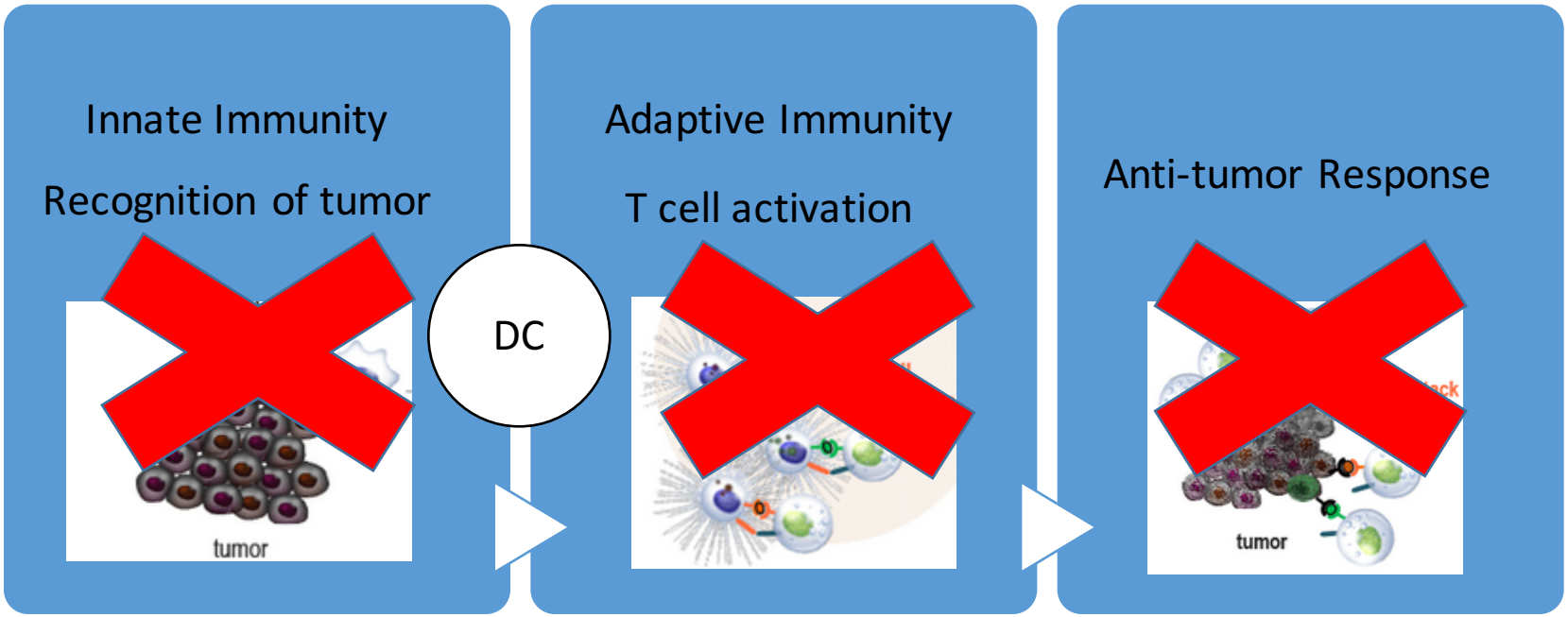





1908 2015

# Immune System and Cancer

## Tolerance



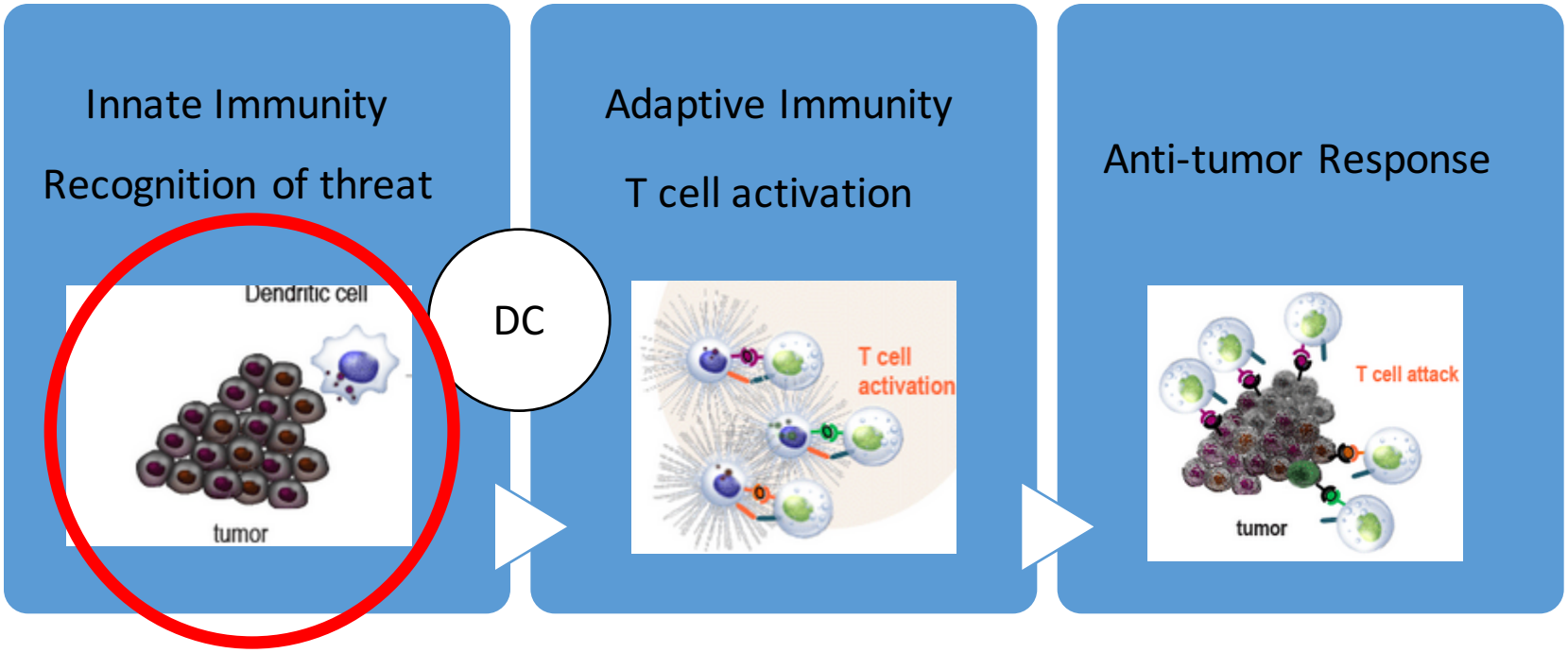

**Defective antigen presentation**

**Inhibition of CTL**

**Immunosuppressive TME**

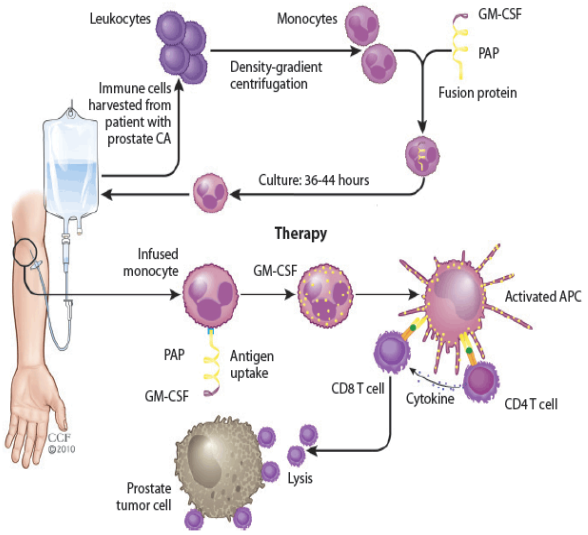
**Combinational approach**

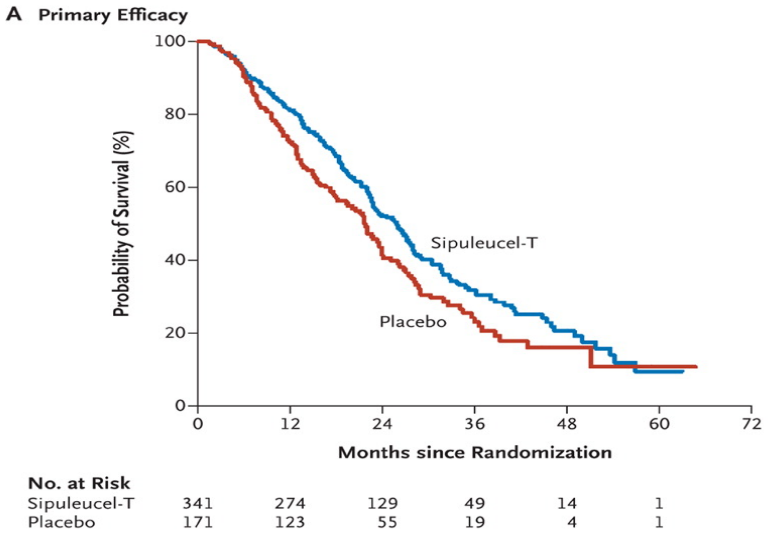
# Vaccine combination



# Sipuleucel-T
# Autologous DC vaccine

- PBMCs collected by leukapheresis
  - Cultured in EX VIVO with PA2024 (fusion protein of PAP and GM-CSF)
- Re-infusion of vaccine product x 3
  - Prime and boost



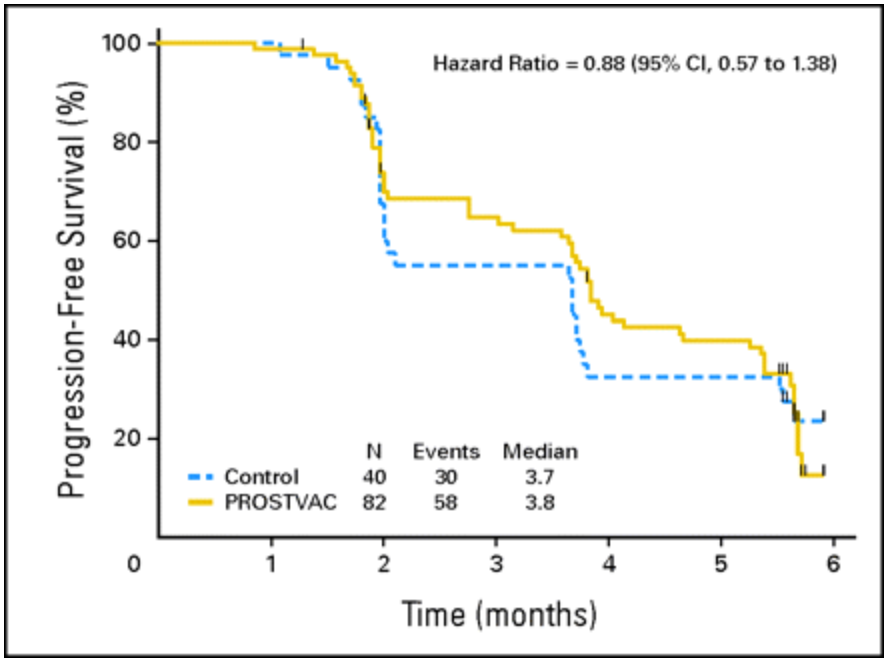



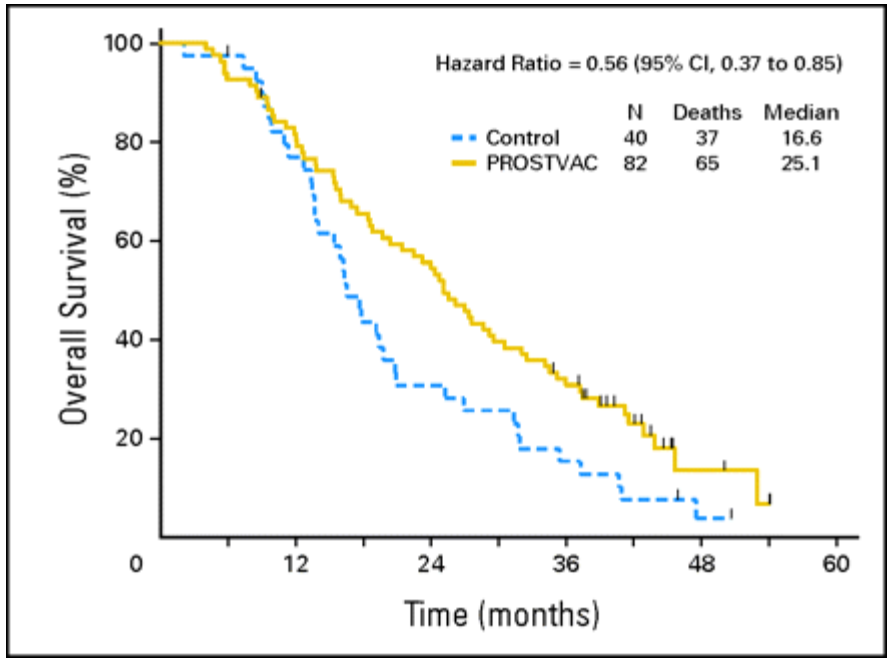

HR 0.775; P .032
(25.8 vs. 21.7)

*No difference in PFS
1 PR
2.6% PSA response (↓ >50%)

Kantoff PW. N Engl J Med 2010

# PROSTVAC-VF



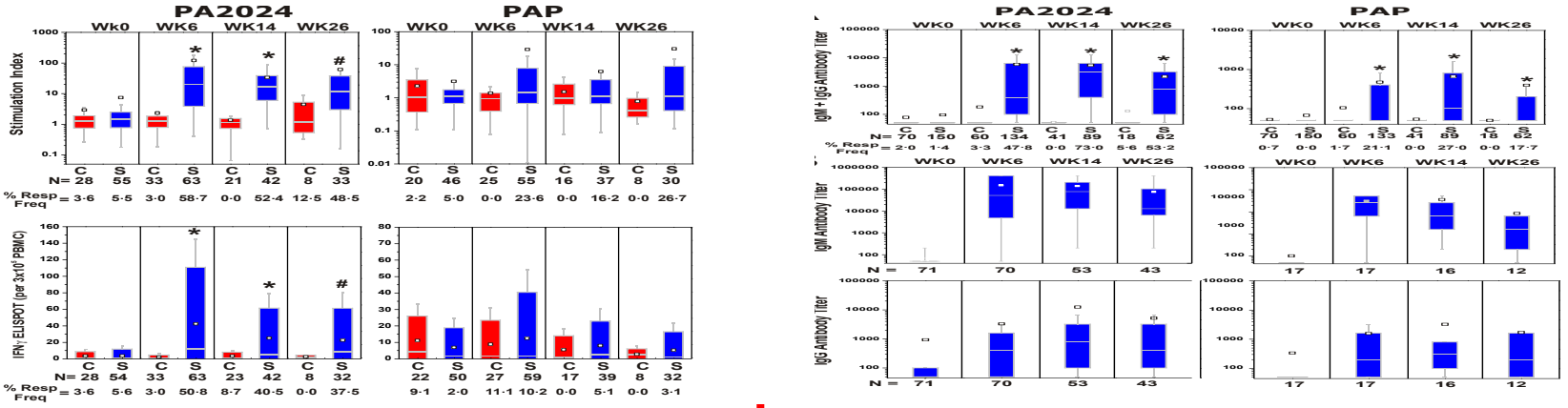

1 PSA response > 80%. No radiographic response

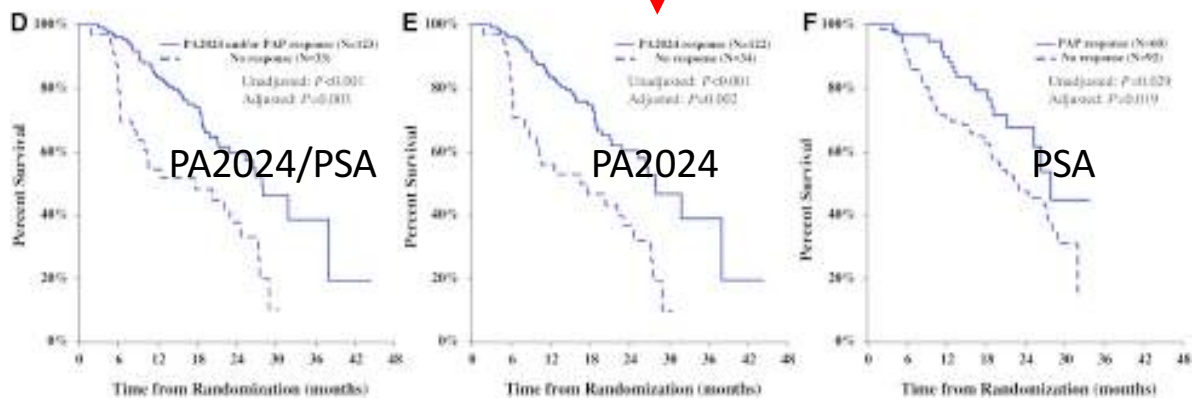
Cancer Immunol Immunother (2013) 62:137–147
DOI 10.1007/s00262-012-1317-2

ORIGINAL ARTICLE

# Sipuleucel-T immune parameters correlate with survival: an analysis of the randomized phase 3 clinical trials in men with castration-resistant prostate cancer

Sip-T induces long-lasting **cellular** and **humoral** immune responses




Sheikh, Cancer Immunol Immunother 2013

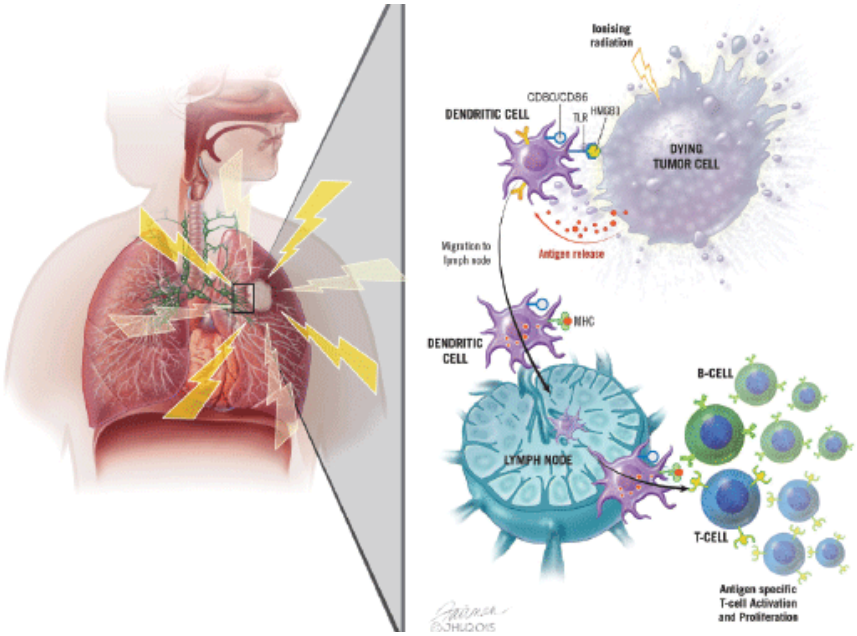
# Hypothesis I

Enhanced sipuleucel-T-induced immune response may translate into better clinical outcome

# Immune Modulation by Radiation

**RT-induced cell death = immunogenic cell death?**

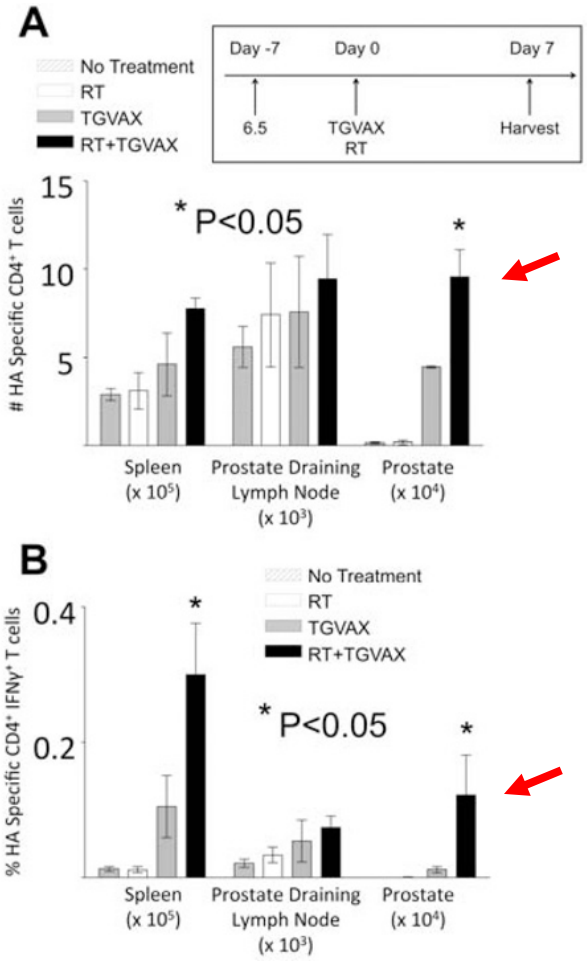
- Release of TAAs
- Enhanced display of TAAs
- Enhanced expression of cell surface molecules
  - MHC class 1, ICAM-1
- Complex effects on TME

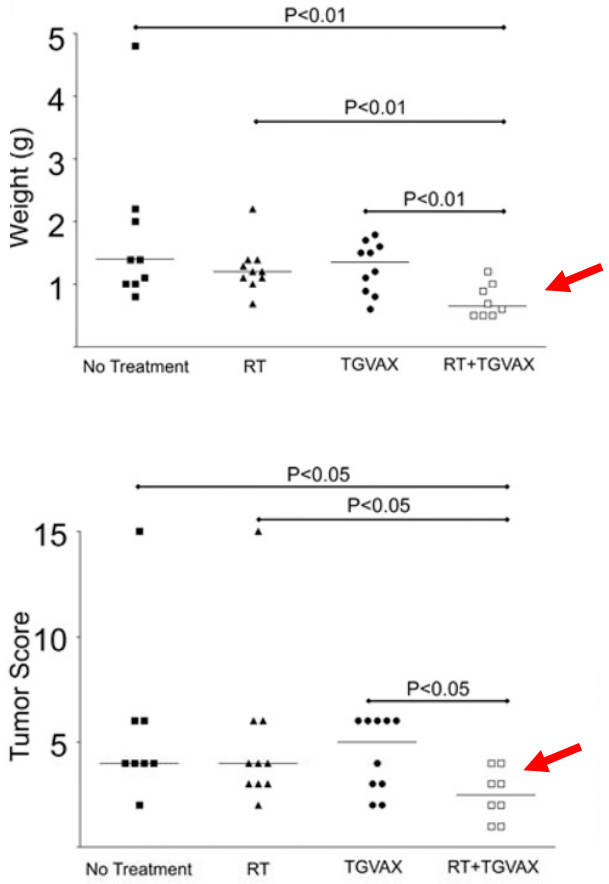



**In-situ personalized "vaccine"**

Sharabi et al Oncology 2015

# In Vivo Evidence of Radiation + Vaccine




Drake et al. Int J Radiat Oncol Biol Phys 2015

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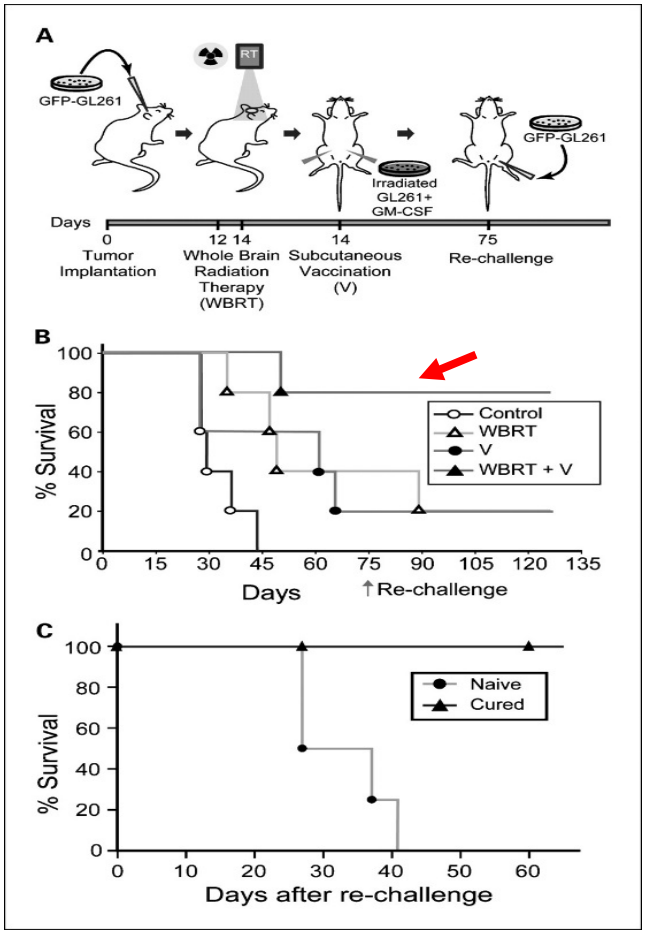



WBRT:
Upregulation of MHC-I
CD4/CD8 T cell tumor infiltration

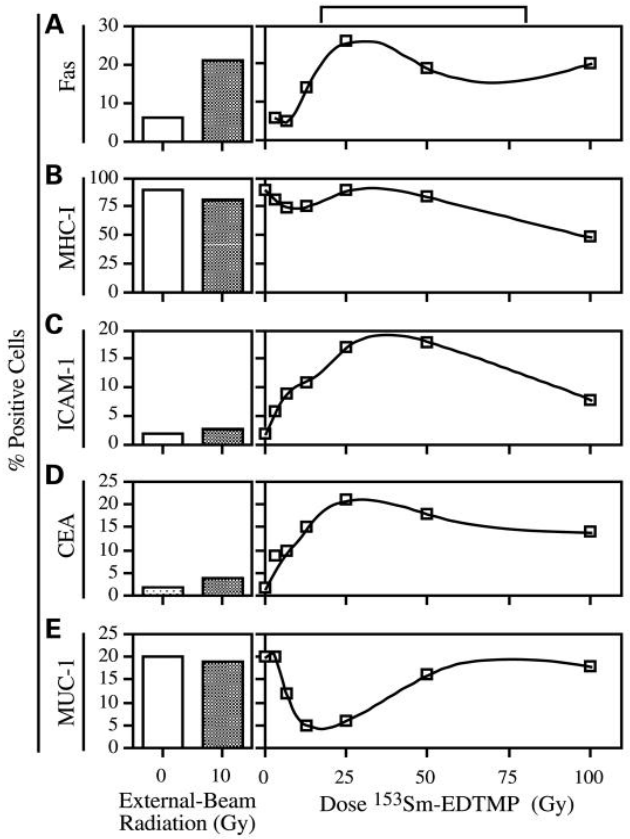
Newcomb et al. Clin Cancer Res. 2006

# Radiation + Vaccine: Clinical trials

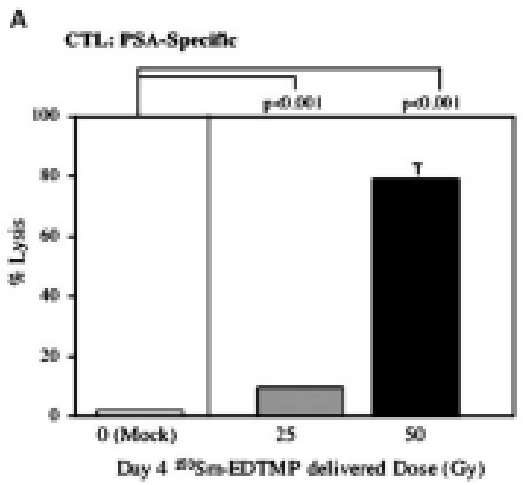
- Phase II Sipuleucel-T + EBRT (NCT01807065): closed
  - Feasibility
- Phase II Sipuleucel-T + SABR (NCT01818986): open
  - Time to progression
- Pilot Sipuleucel-T + EBRT (NCT01833208): open
  - Ag specific T cell activation
- Multicenter Sipuleucel-T + EBRT (NCT02232230): open
  - Ag specific T cell activation

# Immune Modulation by **Radiopharmaceuticals**

$^{153}$Sm-EDTMP




| | 0 Gy | 25 Gy | 50 Gy |
|---|---|---|---|
| Accessory genes | | | |
| *Fas* | 1 | 2 | 2 |
| *ICAM-1* | 1 | 29 | 34 |
| Tumor antigen genes | | | |
| *PSA* | 1 | 2.8 | 2.8 |
| *PSM4* | 1 | 4.2 | 4.6 |
| *PAP* | 1 | 29 | 36 |
| *CEA* | 1 | 10 | 13 |
| *MUC-1* | 1 | 3.7 | 2.9 |




Chakraborty et al. Clin Cancer Res. 2008

# Radiopharmaceutical + Vaccine

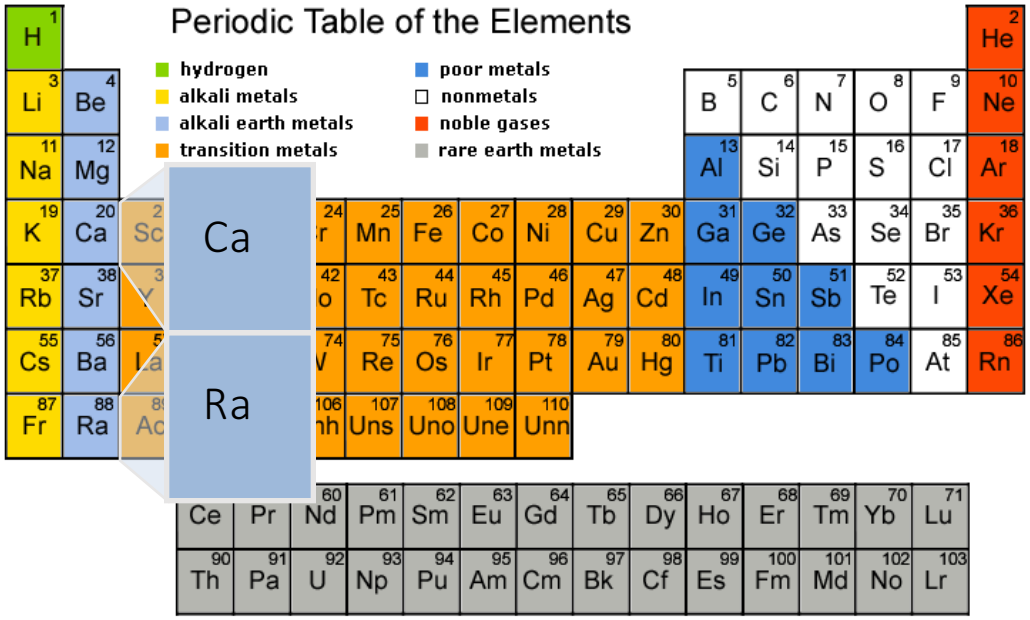
## Phase II samarium-153 EDTMP (Sm-153) +/- PROSTVAC vaccine

| | Sm-153 | Sm-153 + PSA-TRICOM | |
|---|---|---|---|
| **PFS** | | | |
| **At 4 mo** | 3/18 (16.7%) | 8/21 (38.1%) | p=0.13 |
| **mPFS (mo)** | 1.7 | 3.7 | HR=0.48, p=0.034 |
| **PSA decline** | | | |
| **≥ 30%** | 0 | 4/21 (19.0%) | p=0.073 |
| **≥ 50%** | 0 | 2/21 (9.5%) | p=0.283 |

Sm-153 on D#8 and then Q12 weeks +/- PSA-TRICOM on D# 1, 15, 29, then Q4 weeks
Early closure of this trial due to poor accrual after 44 pts

Heery et al. GU ASCO 2013

# Radium-223


Periodic Table of the Elements
hydrogen
alkali metals
alkali earth metals
transition metals
poor metals
nonmetals
noble gases
rare earth metals
Ca
Ra

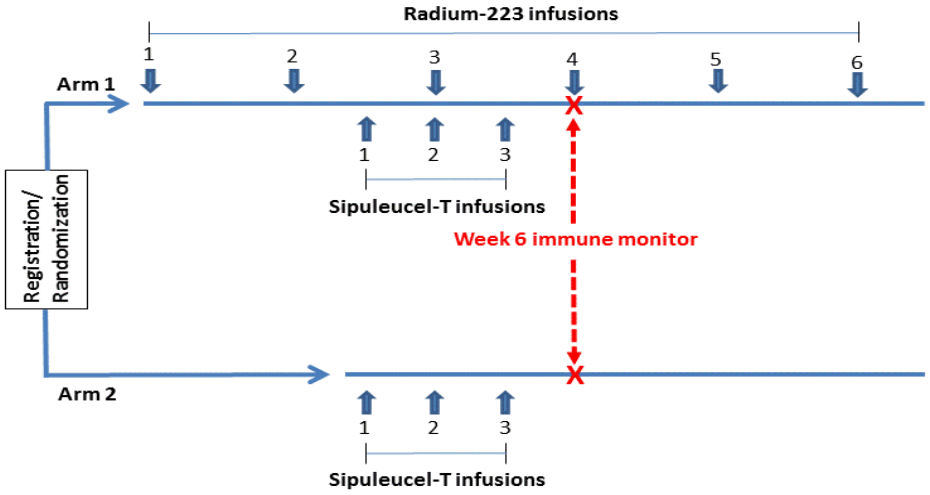
# Hypothesis II

Enhanced sipuleucel-T induced immune response may translate into better clinical outcome

Combined radium-223 may enhance sipuleucel-T induced immune response

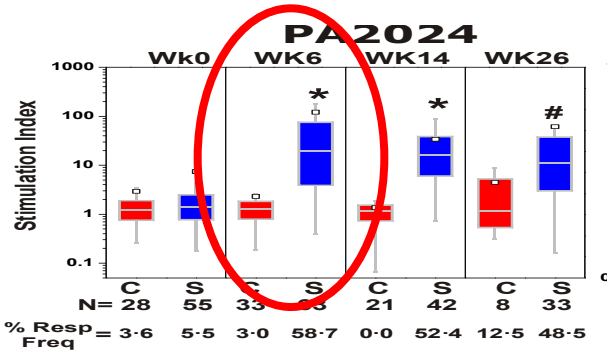
# Phase II Study of Sipuleucel-T with or without Radium-223

mCRPC with
no or minimal Sx




1’ Objective:
To determine whether Rad-223 to sipuleucel-T enhances i

1’ Endpoint:
**PA2024-specific T-cell proliferation** at 6 weeks after 1st sip



# Phase II Study of Sipuleucel-T with or without Radium-223

## 2’ Clinical Endpoints

- Safety (CTCAE v4.0 )
- PSA progression (PCWG2)
- Radiographic progression (RECIST/PCWG2)
- Pain progression (Use of opioid analgesics )
- Occurrence of first SRE
- First chemotherapy use

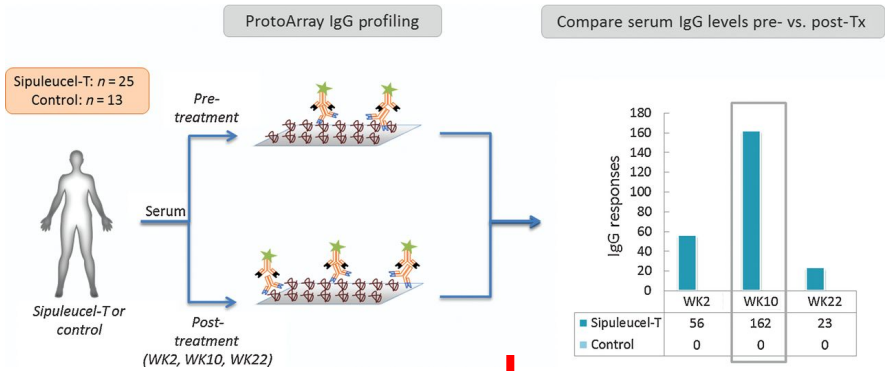
# Phase II Study of Sipuleucel-T with or without Radium-223

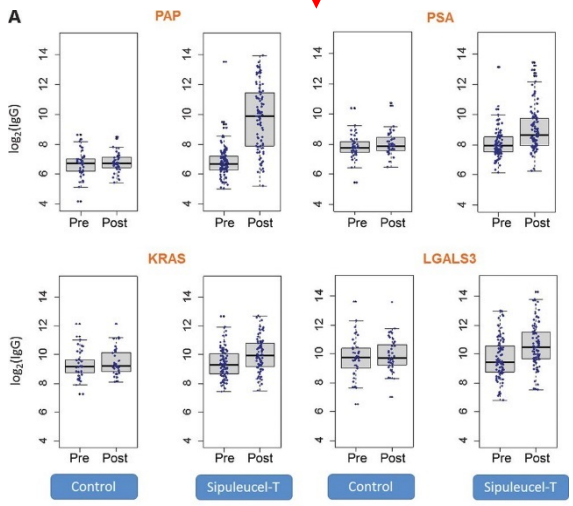
## 2' Immune Endpoints

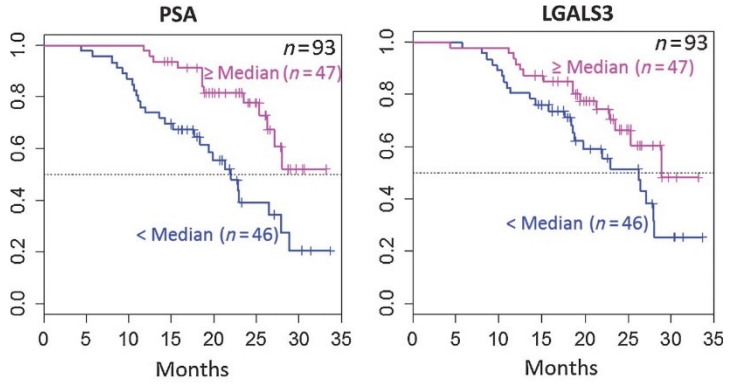
- PA2024-and PAP-specific T-cell proliferation
  - 3H-thymidine assay
- PA2024-and PAP-specific T-cell activation
  - IFNγ ELISPOT
- PA2024-and PAP-specific Ab (IgM/IgG) response
  - ELISA
- Sipuleucel-T induced antigen (epitope) spread
  - IgG responses to off-target Ags (Protein microarray)
- Product immune parameters

Clinical Cancer Research

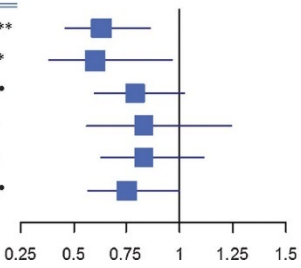
# Humoral Immune Response against Nontargeted Tumor Antigens after Treatment with Sipuleucel-T and Its Association with Improved Clinical Outcome



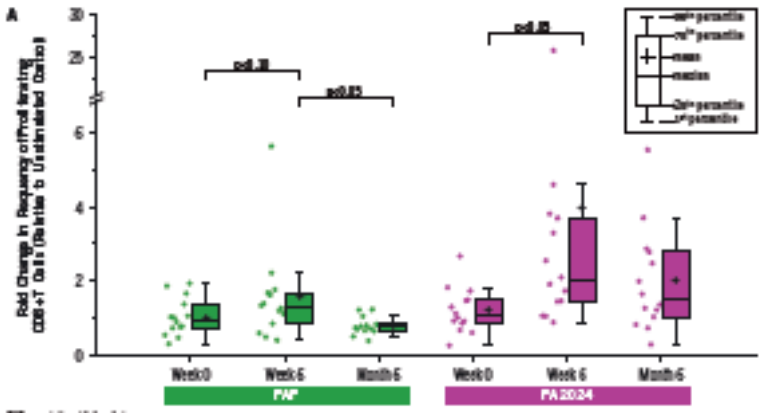

| Antigen | HR | P |
|---|---|---|
| PSA | 0.63 | 0.003** |
| LGALS3 | 0.60 | 0.035* |
| ERAS | 0.79 | 0.075• |
| LGALS8 | 0.83 | 0.369 |
| KRAS | 0.83 | 0.218 |
| KLK2 | 0.75 | 0.051• |

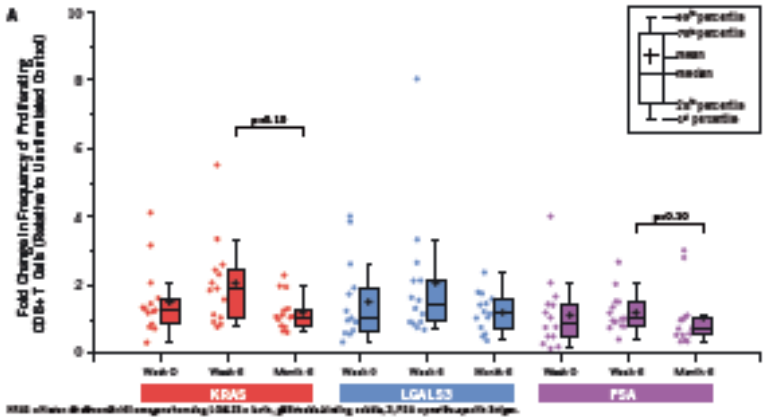



GuhaThakurta and Drake et al. Clin Cancer Res 2015

# Sipuleucel-T induced Antigen Spread
## CD8 T cell responses to secondary antigens

- PBMCs obtained from STAND (n=10) and STRIDE (n=4) trial
- CD8 T cell proliferation to secondary antigens
  - KRAS, LGALS3, PSA
  - At baseline, week 6, and month 6

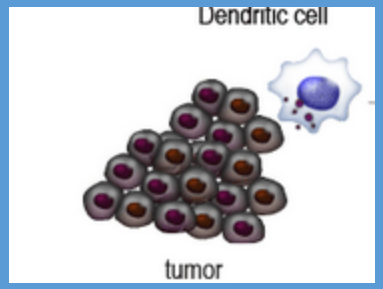


# Immune Checkpoint

Innate Immunity

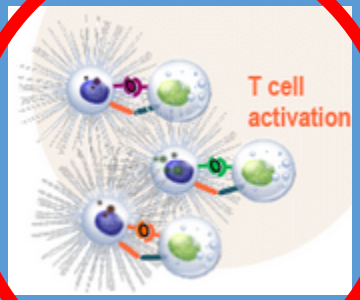
Recognition of threat



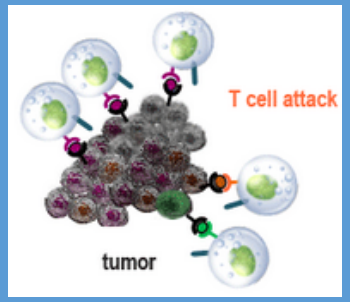

DC

Adaptive Immunity

T cell activation




Anti-tumor Response



# Atezolizumab vs. Pambrolizumab vs. Avelumab

## Post-platinum mUC

| Agents | PD-L1 IHC | | ORR |
|---|---|---|---|
| | Cell types | Stain (Cut-off) | |
| Atezolizumab (Anti-PD-L1) | TIL | + (≥5%) | 50% |
| | | - (<5%) | 17% |
| Pembrolizumab (Anti-PD1) | Tumor/TIL | + | 29% |
| | | - | 0% |
| | Tumor | + | 33% |
| | | - | 9% |
| Avelumabb (Anti-PD-L1) | Tumor | + (≥5%) | 40% |
| | | - (<5%) | 9% |

Petrylak et al. ASCO 2015, Plimack al. ASCO 2015, Apolo et al. GU ASCO 2016

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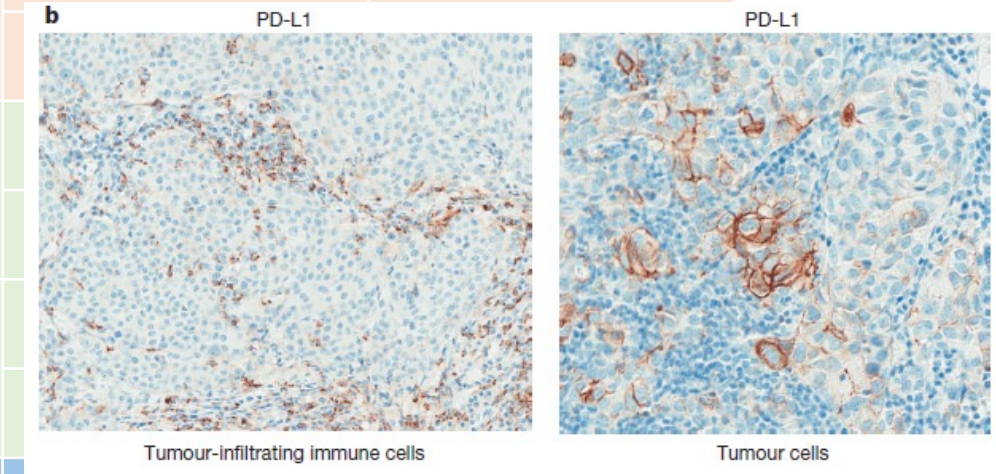
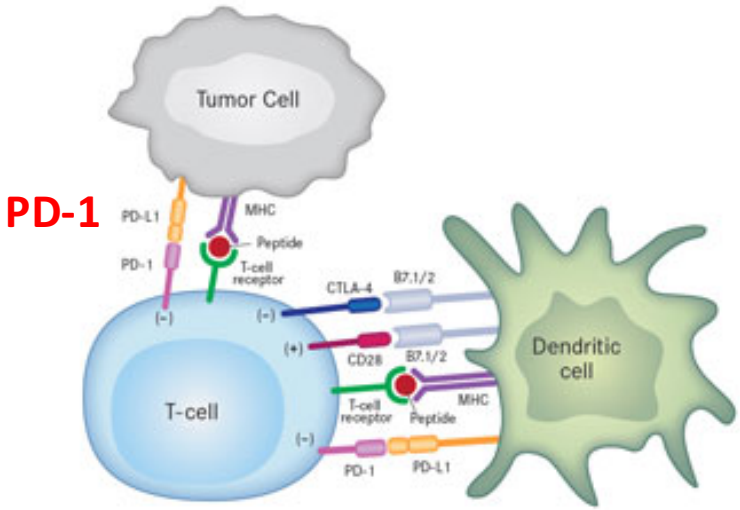
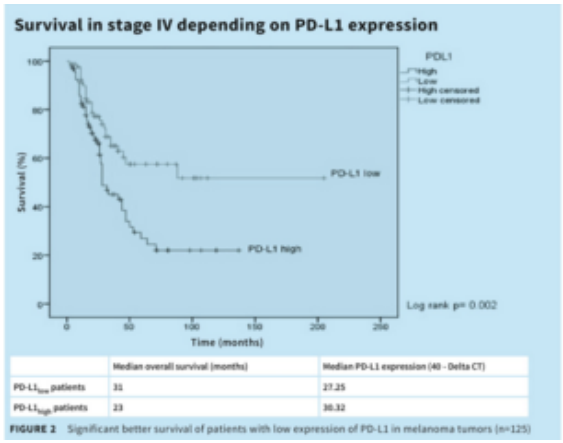
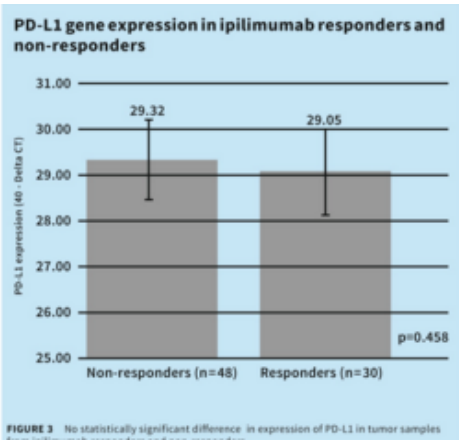



Petrylak et al. ASCO 2015, Plimack al. ASCO 2015, Apolo et al. GU ASCO 2016

# Dual Immune Checkpoint Inhibition: Anti-PD-1/PD-L1 + Anti-CTLA-4




Bruggemann et al. ASCO 2015

# Dual Immune Checkpoint Inhibition PD-1/PD-L1 +/- CTLA-4

| Author | Population | Agent | Target | PD-L1+ ORR | PD-L1- ORR |
|---|---|---|---|---|---|
| Petrylak | mUC | Atezolizumab | PD-L1 | 50% | 17% |
| Herbst | mSolid Tumors | Atezolizumab | PD-L1 | 34% | 16% |
| McDermott | mRCC | Atezolizumab | PD-L1 | 20% | 10% |
| Horn | mNSCLC | Atezolizumab | PD-L1 | 45% | 14% |
| Plimack | mUC | Pembrolizumab | PD-1 | 33% | 9% |
| Daud | mMel | Pembrolizumab | PD-1 | 53% | 6% |
| Garon | mNSCLC | Pembrolizumab | PD-1 | 45% | 17% |
| Choueiri | mRCC | Nivolumab | PD-1 | 22% | 8% |
| Brahmer | mNSCLC | Nivolumab | PD-1 | 15% | 14% |
| Callahan | mMel | Nivolumab + Ipilimumab | PD-1/CTLA-4 | 41% | 46% |
| Hammers | mRCC | Nivolumab + Ipilimumab | PD-1/CTLA-4 | 50% | 55% |
| Larkin | mMel | Nivolumab + Ipilimumab | PD-1/CTLA-4 | 72% | 58% |
| Grasso | mMel | Nivolumab | PD-1 | 44% | 17% |
| Topalian | mSolid Tumors | Nivolumab | PD-1 | 36% | 0% |

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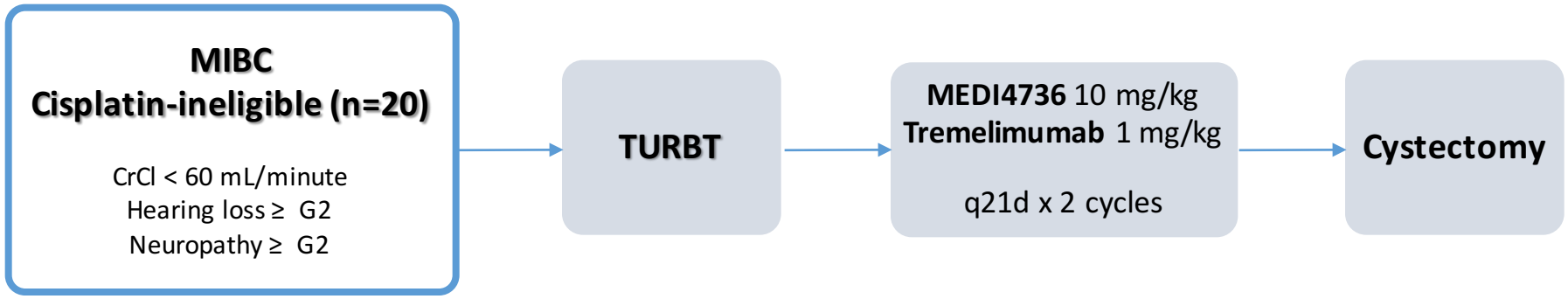



**Primary Endpoint:**

- Tumor infiltrating CD8+ T-cell at cystectomy after MEDI4736/tremelimumab

**Secondary Endpoints:**

- Safety and antitumor efficacy of MEDI4736/tremelimumab

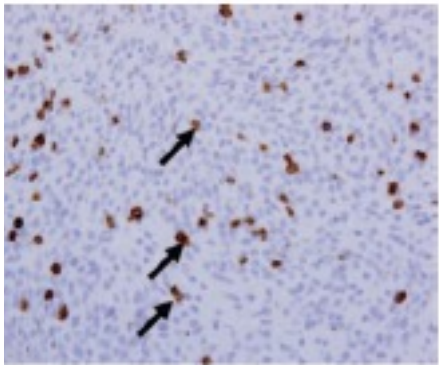
**Exploratory Endpoints:**

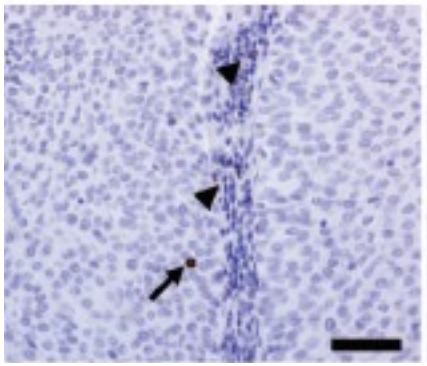
- Characterization of tumor tissue and peripheral lymphocytes
- Analysis of soluble immune markers (cytokines/chemokines)
- Analysis of tumor and blood genetic and epigenetic profiles
- Assessment of T-cell repertoire

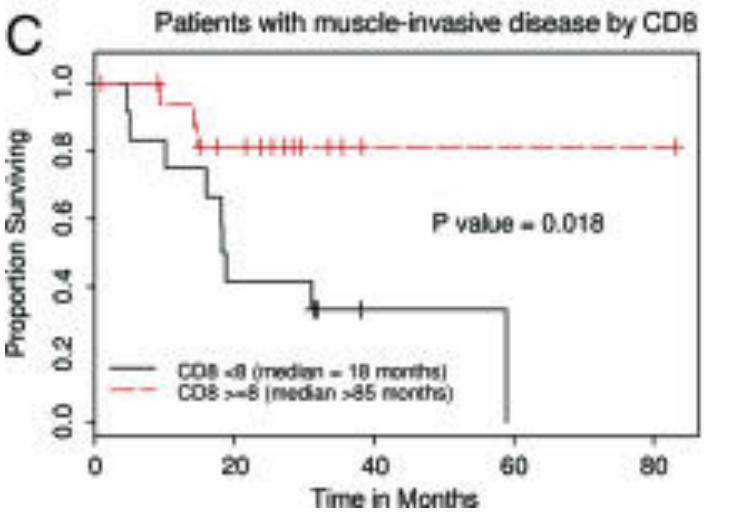
# Tumor Infiltrating Lymphocyte (TIL): prognostic marker?

Intratumor vs. margin/stroma? TIL vs. subtype? density vs % vs. ratio?

- The presence of TILs associated with improved survival in MIBC (n=154)
- ↑ CD8+ TILs (≥ 8/0.0625 $mm^2$) correlated with better survival in MIBC (N=69)



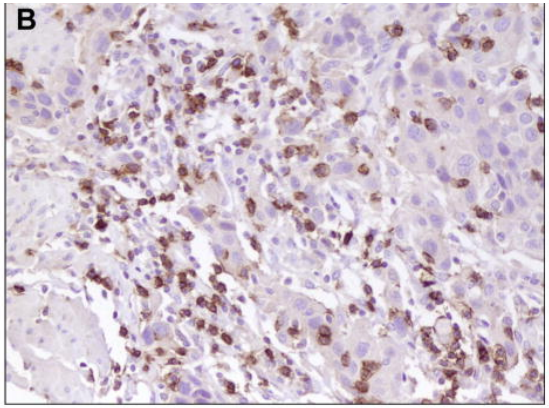





**8/0.0625 $mm^2$ ≈ 4/100 tumor cells**

Lipponen et al. Eur J Cancer. 1992,
Sharma et al. PNSA 2007

# Tumor Infiltrating Lymphocyte (TIL): prognostic marker?




| | Overall Survival | | Disease-specific Survival | |
|---|---|---|---|---|
| **CD8 Density** | **OR (95% CI)** | ***P* Value** | **OR (95% CI)** | ***P* Value** |
| Unadjusted | 0.12 (0.02–0.68) | .02 | 0.14 (0.03–0.78) | .02 |
| Adjusted for demographic parameters* | 0.1 (0.02–0.69) | .02 | 0.06 (0.01–0.53) | .01 |
| Adjusted for pathologic parameters† | 0.1 (0.01–0.69) | .02 | 0.05 (0.01–0.62) | .02 |
| Adjusted for neoadjuvant therapy‡ | 0.04 (0.004–0.46) | .01 | 0.1 (0.02–0.6) | .01 |
| Adjusted for intravesical therapy | 0.09 (0.01–0.58) | .01 | 0.11 (0.02–0.7) | .02 |

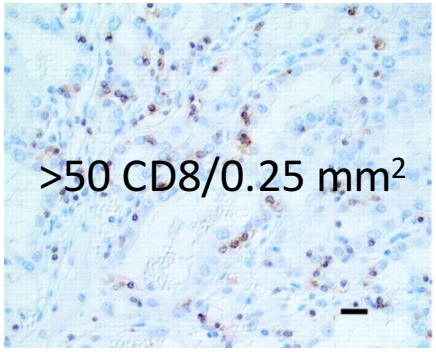
Intratumoral CD8+ T cells (400x)

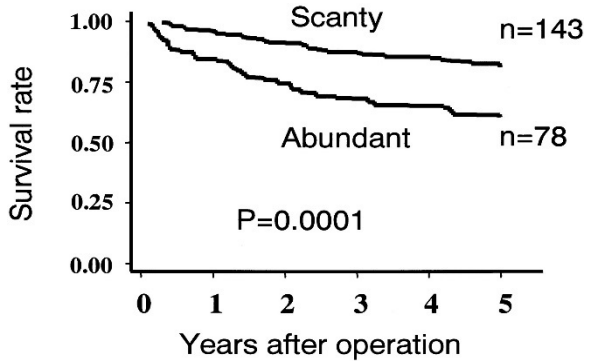
High CD8 density: **≥60 CD8+/HPF**: 11/56 (19.6%): intratumoral (n=56)

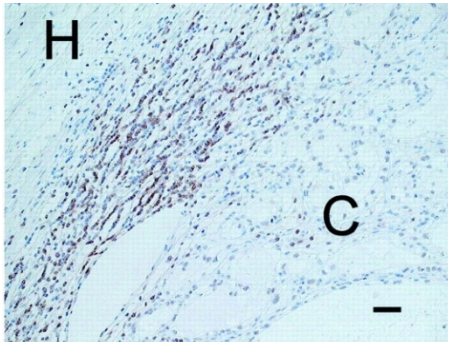
Drake, and Netto et al. Urology 2015

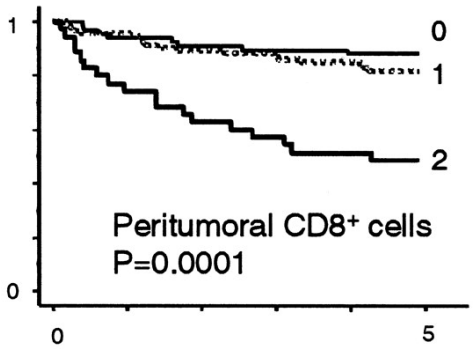
# Tumor Infiltrating Lymphocyte (TIL): prognostic marker?

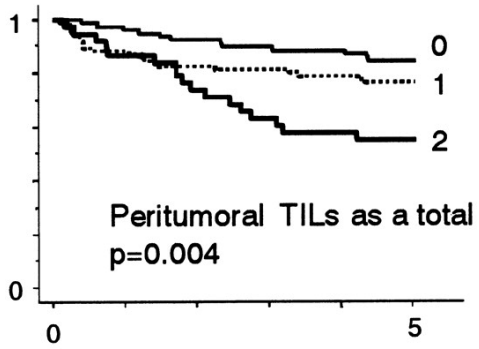
Paradoxical correlation of $CD8^+$ T-cell infiltration with poor prognosis



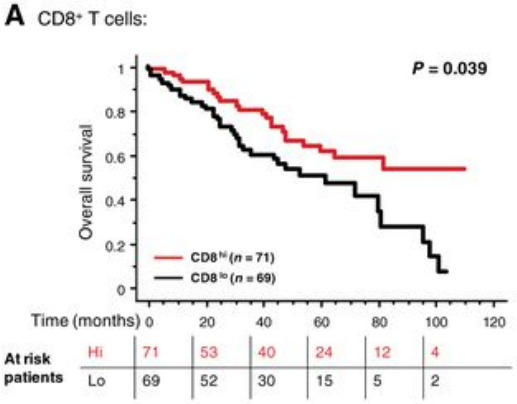



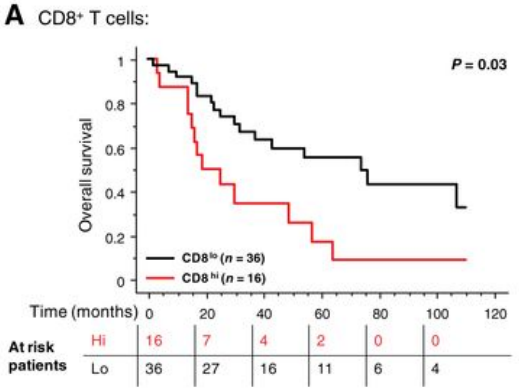




Nakano et al. Cancer Res 2001

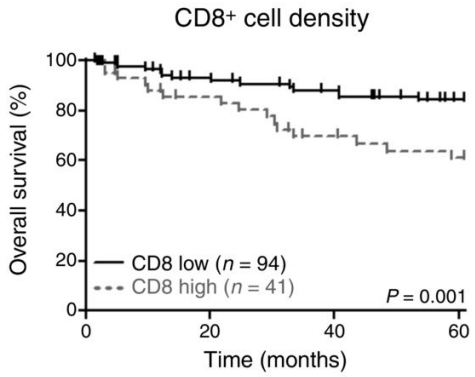
# Tumor Infiltrating Lymphocyte (TIL): prognostic marker?



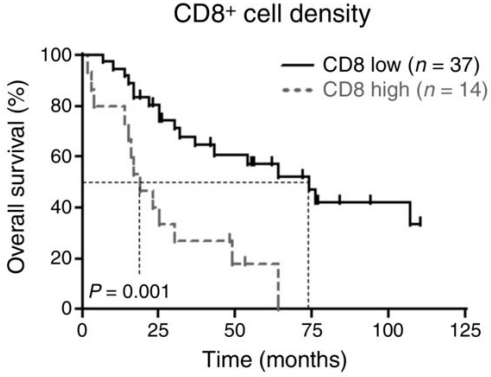

Colon cancer lung mets




RCC lung mets



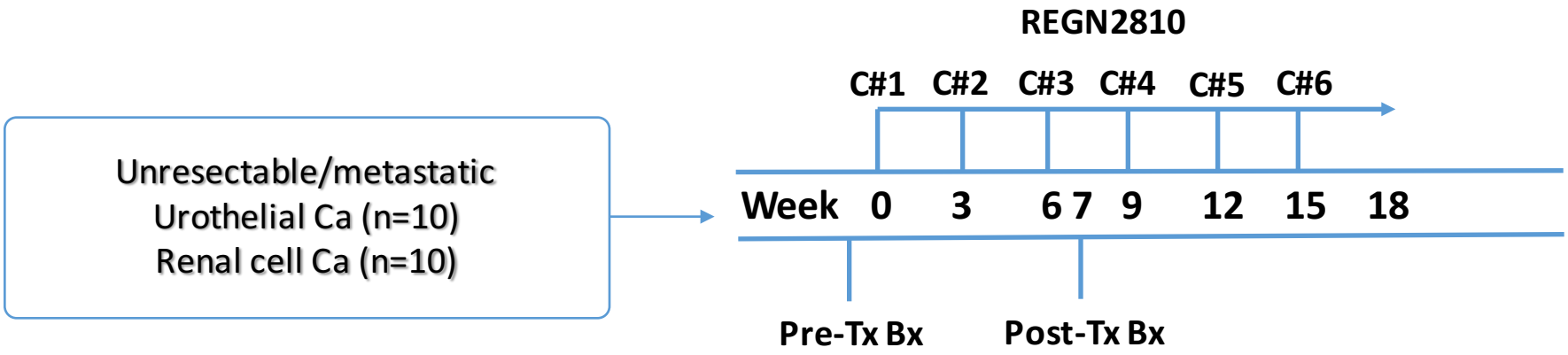

Primary RCC tumor




RCC Lung mets

Remark et al. Clin Cancer Res 2013
Giraldo et al. Clin Cancer Res 2015

# Immune Predictive Biomarker Pharmacodynamics



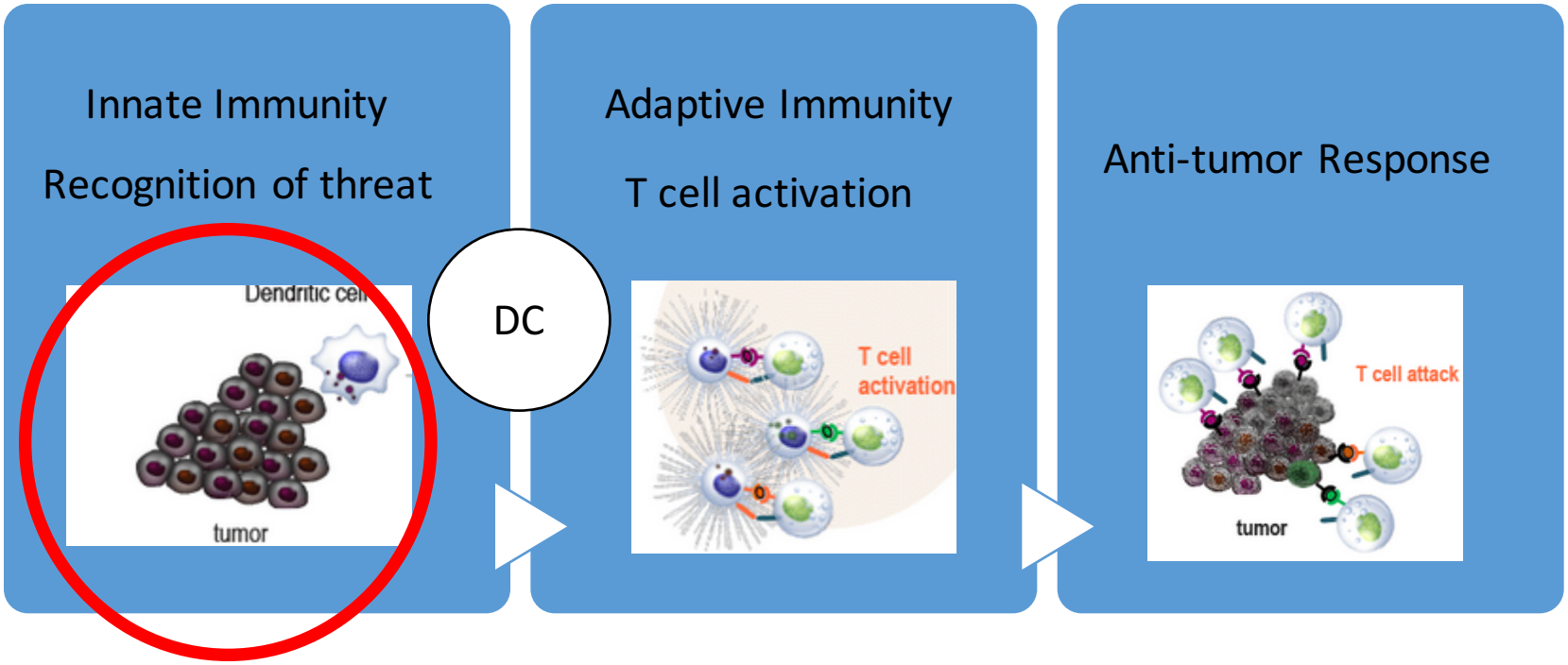

TIL: CD8 density vs. CD8 delta vs. CD8/Treg ratio vs. Other
Immune gene expression signature (velocity?)
PD-L1 expression
TCR clonality
Mutational burden
MMR gene (microsatellite instability)
Prognostic vs predictive?

# Dual Immune Checkpoint Inhibition

| Author | Population | Agent | Target | PD-L1+ ORR | PD-L1- ORR |
|---|---|---|---|---|---|
| Petrylak | mUC | Atezolizumab | PD-L1 | 50% | 17% |
| Herbst | mSolid Tumors | Atezolizumab | PD-L1 | 34% | 16% |
| McDermott | mRCC | Atezolizumab | PD-L1 | 20% | 10% |
| Horn | mNSCLC | Atezolizumab | PD-L1 | 45% | 14% |
| Plimack | mUC | Pembrolizumab | PD-1 | 33% | 9% |
| Daud | mMel | Pembrolizumab | PD-1 | 53% | 6% |
| Garon | mNSCLC | Pembrolizumab | PD-1 | 45% | 17% |
| Choueiri | mRCC | Nivolumab | PD-1 | 22% | 8% |
| Brahmer | mNSCLC | Nivolumab | PD-1 | 15% | 14% |
| Callahan | mMel | Nivolumab + Ipilimumab | PD-1/CTLA-4 | 41% | 46% |
| Hammers | mRCC | Nivolumab + Ipilimumab | PD-1/CTLA-4 | 50% | 55% |
| Larkin | mMel | Nivolumab + Ipilimumab | PD-1/CTLA-4 | 72% | 58% |
| Grasso | mMel | Nivolumab | PD-1 | 44% | 17% |
| Topalian | mSolid Tumors | Nivolumab | PD-1 | 36% | 0% |

Hammers et al. ASCO 2014

# Immune System and Cancer

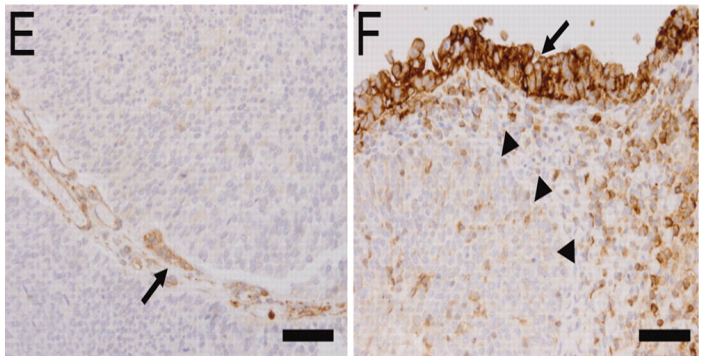


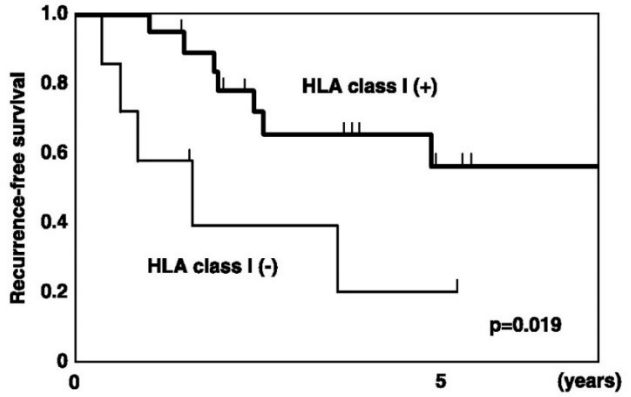

**Loss/down-regulation of MHC I**

Loss/masking of TAAs

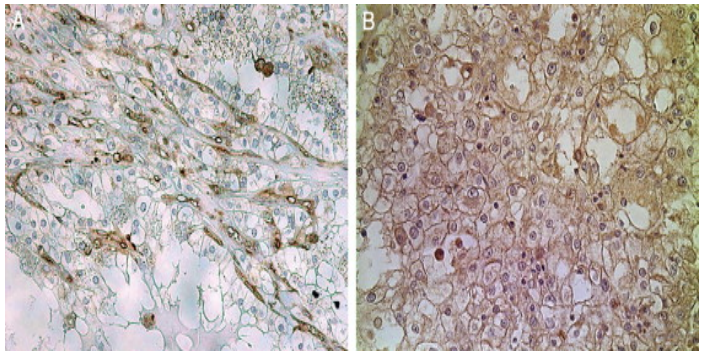
# Failed antigen presentation: MHC (HLA) I downregulation

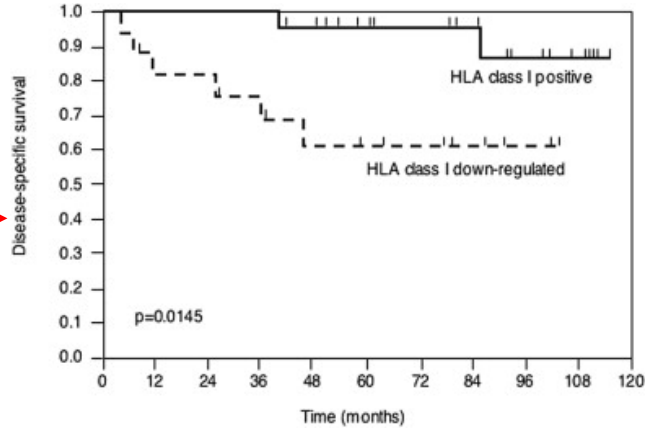
Bladder




RCC




Sharma et al.PNSA 2007, Kitamura et al. J Urol 2007, Kitamura et al. J Urol 2006

# Innate Immunity


Cytotoxicity **in the absence of MHC/Ag complex**

# NK Cells

- Rc-based recognition of "**abnormal cell**"
  - Missing-self: loss of MHC I
  - Non-self: pathogen-encoded molecules
  - Stressed-self: stress-induced ligands
- Tumor immune surveillance
  - Direct tumor cell cytotoxicity
    - Perforin and granzymes-dependent necrosis
    - Death Rc-mediated apoptosis (TRAIL, FasL)
  - Bridge to adaptive immune response
    - Release of cytokines and chemokines
    - Recruitment of other accessory/effector immune cells

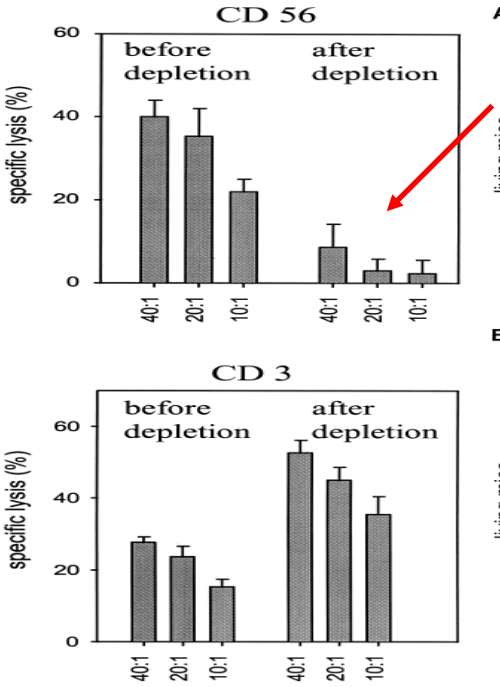
# Role of NK Cells in Antitumor Response

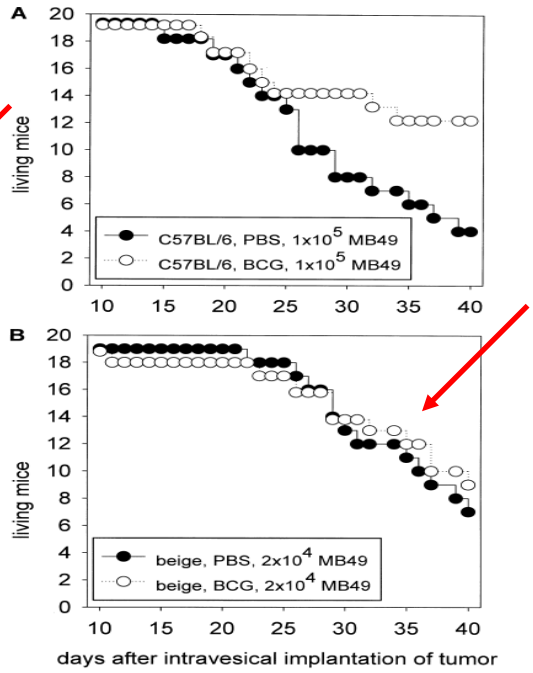
**Bladder**

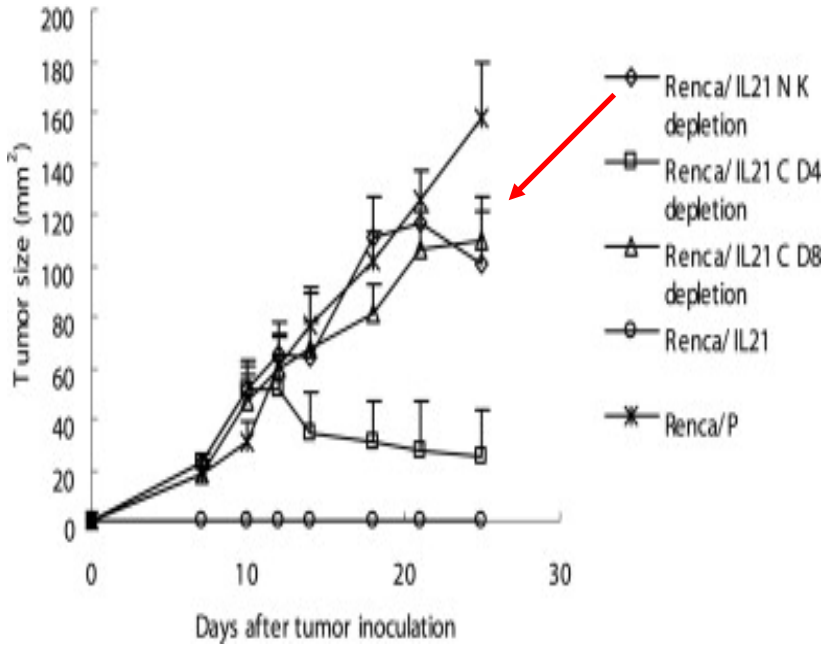
**RCC**

**NK cell** depletion

NK-WT mice




**T-cell** depletion

**NK cell deficient** beige mice

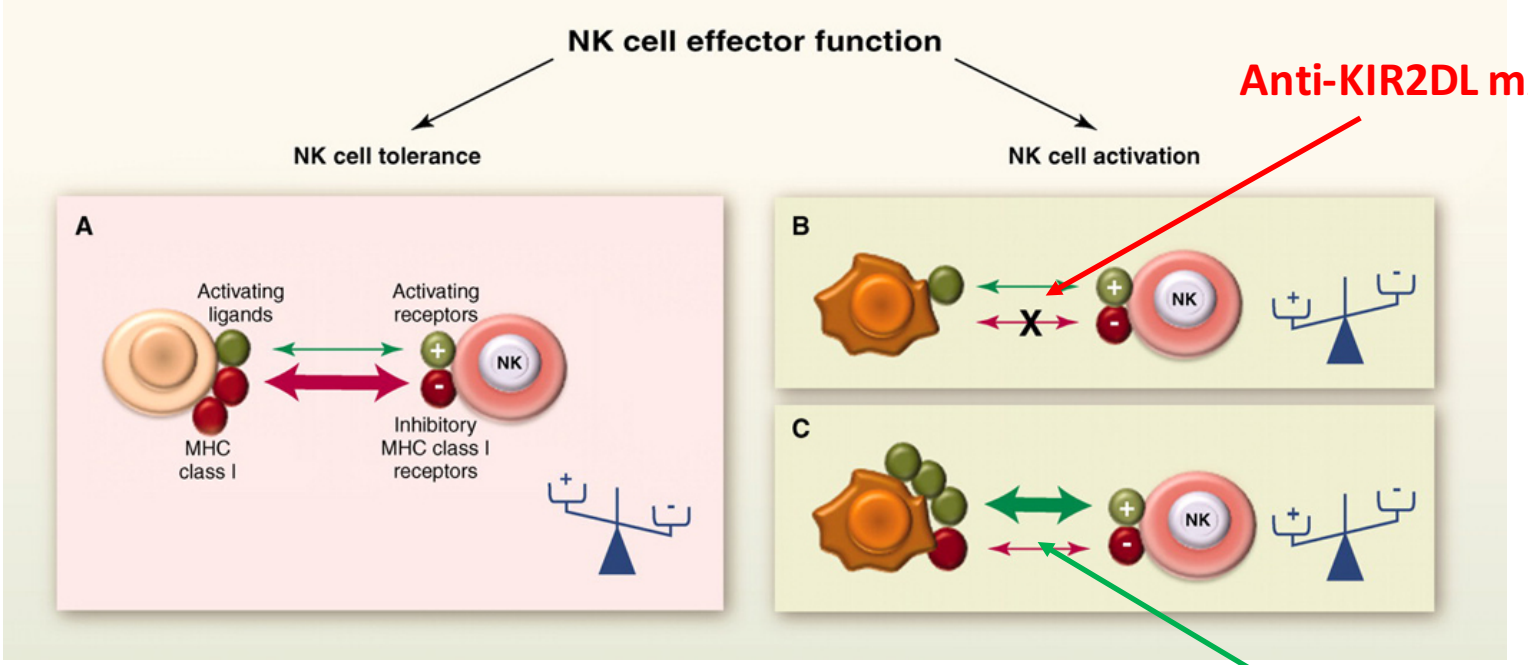
Bladder BCG therapy

RCC IL-21 therapy

Brandau. Int J Cancer. 2001, Kumano et al. J Urol2007

# NK Cell Activity

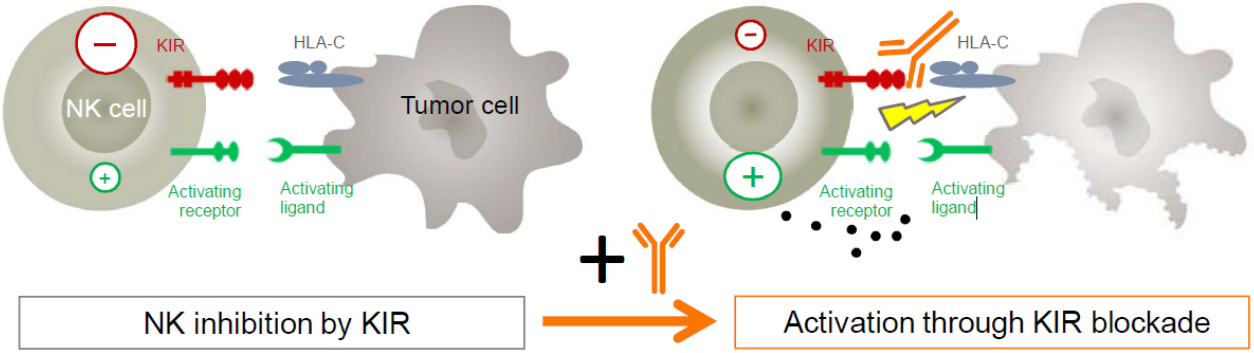
Balance of activating and inhibitory Rc stimulation




Vivier. Science. 2011

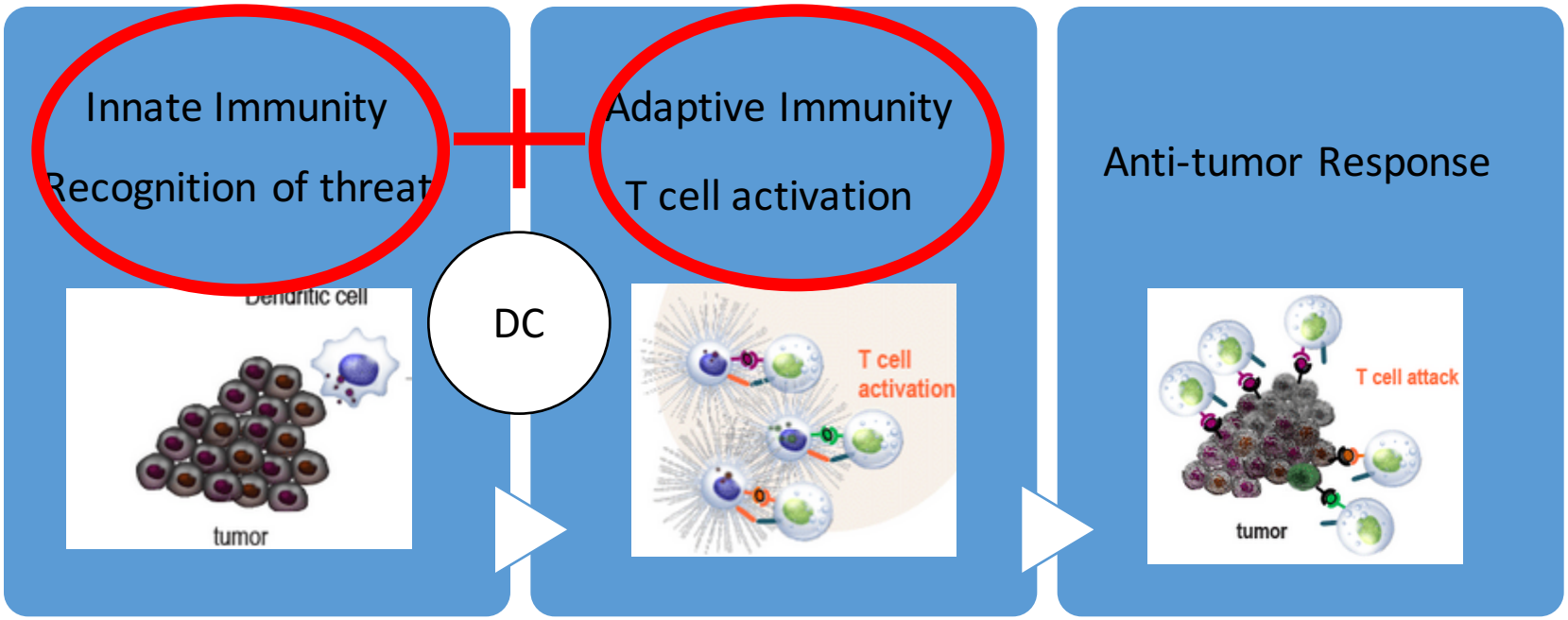
# Killer cell Ig-like Receptors (KIRs): KIR2DL: Inhibitory Rc

- MHC I-specific receptors: inhibitory vs activating
  - **KIR2DL** (1/2/3) interacts with HLA-C allotypes
  - KIR3DL interacts with HLA-A and B allotypes
- KIR/HLA interaction determines the responsiveness
- NK cells preferentially kill cells with low MHC I




Lirirumab

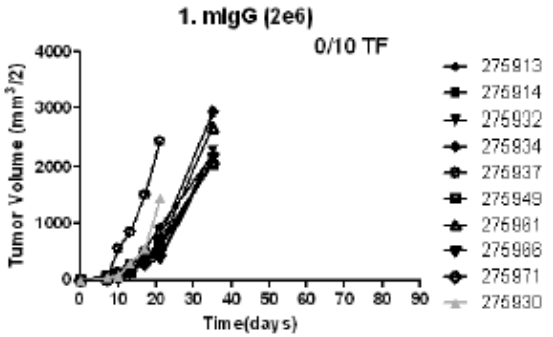
# Combination of **Adaptive** and **Innate** Immunity

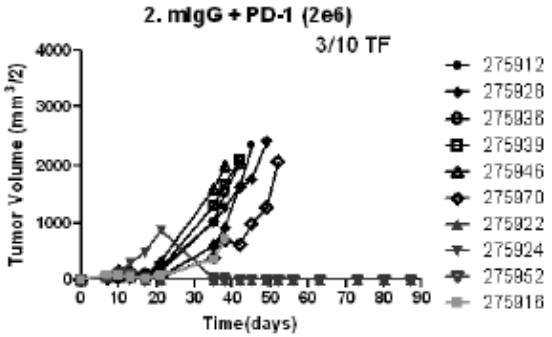


# Combination of **Adaptive** and **Innate** Immunity Anti-PD-1 and KIR mAB

**Figure 1-1: Anti-PD-1 and Anti-KIR in MC38 Murine Colon Carcinoma Model**

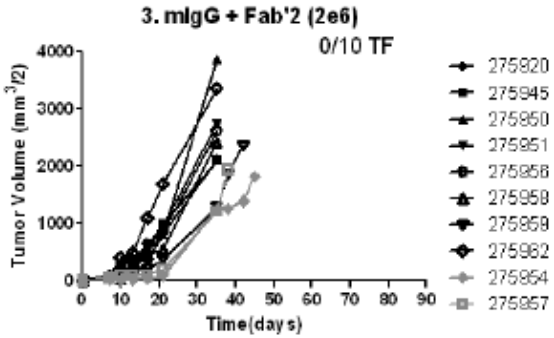
Control

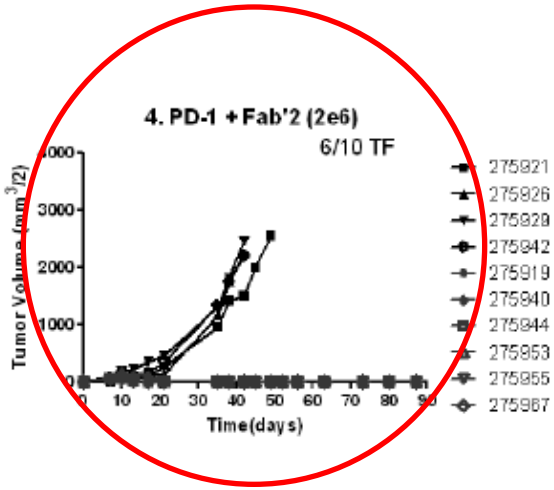



Anti-PD-1 mAB

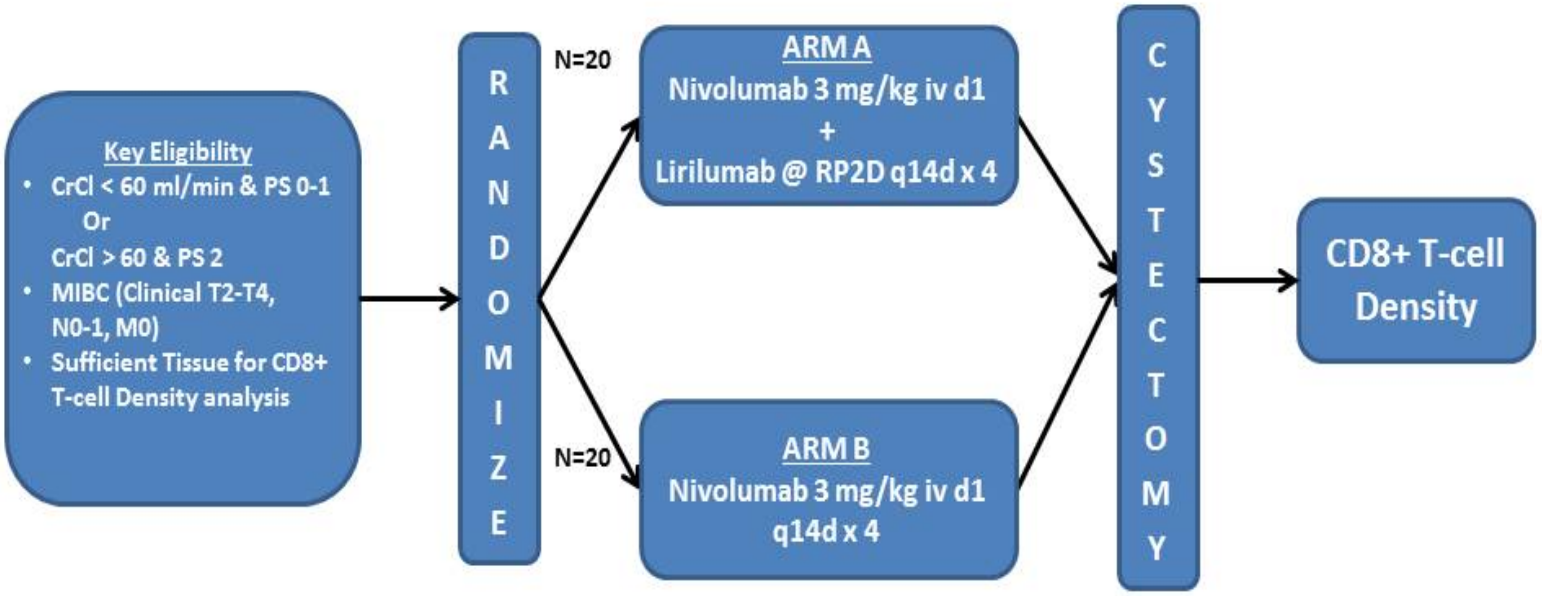
Anti-KIR mAB




Anti-PD-1 mAB
Anti-KIR mAB

# Phase II Nivolumab + Lirilumab



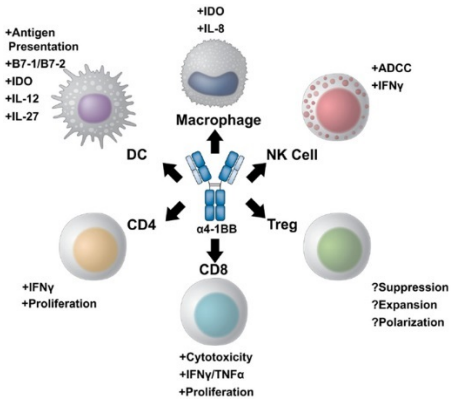

**Primary Endpoint:**

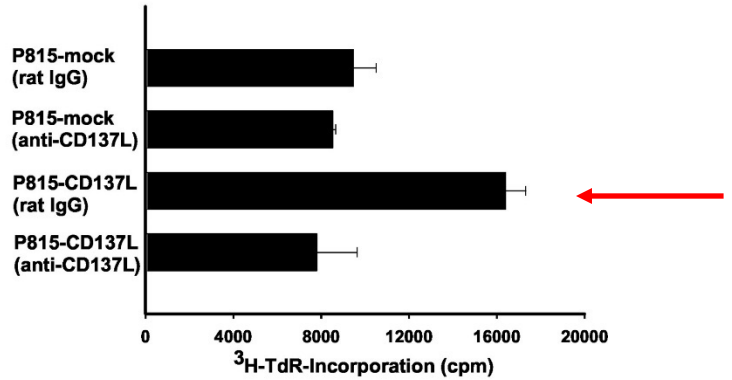
- Tumor infiltrating CD8+ T-cell at cystectomy after

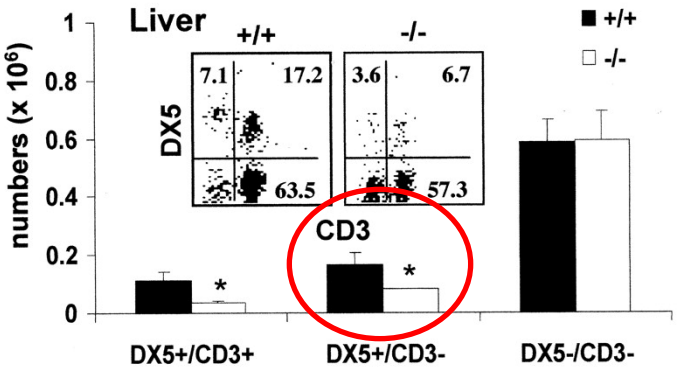
**Secondary Endpoints:**

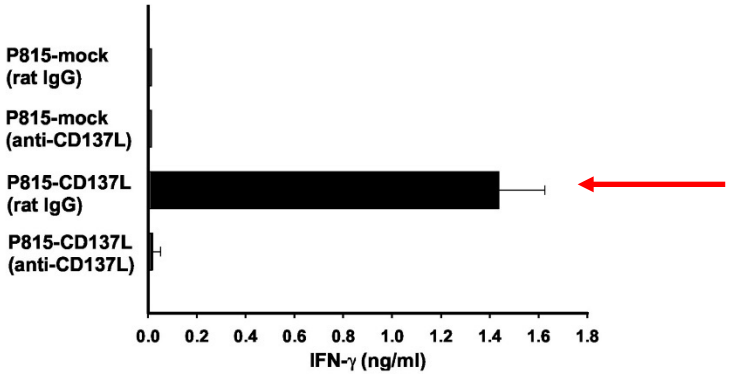
- Safety and antitumor efficacy (the rate of < pT2N0)
- Immunologic Biomarkers and clinical association:
  Peripheral/tissue lymphocyte subsets, cytokine, PD-L1, KIR2DL1/2/3 expression

# 4-1BB (CD137): Co-stimulatory Rc: Urelumab



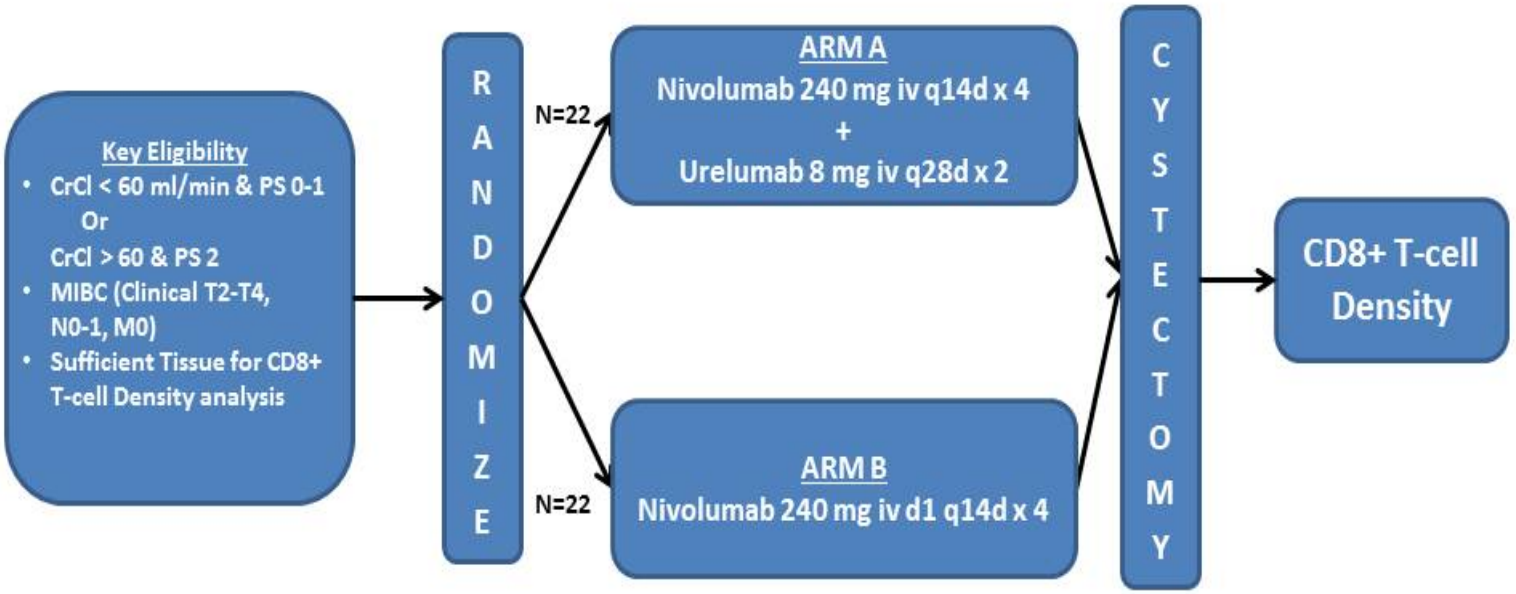




Vinay et al. J Immunol 2004
Wilcox et al. J Immunol 2002

# Phase II Nivolumab + Urelumab

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- Safety and antitumor efficacy (the rate of < pT2N0)
- Immunologic Biomarkers and clinical association:
  Peripheral/tissue lymphocyte subsets, cytokine, PD-L1, KIR2DL1/2/3 expression

# Selective Ongoing Combination Immunotherapy Trials

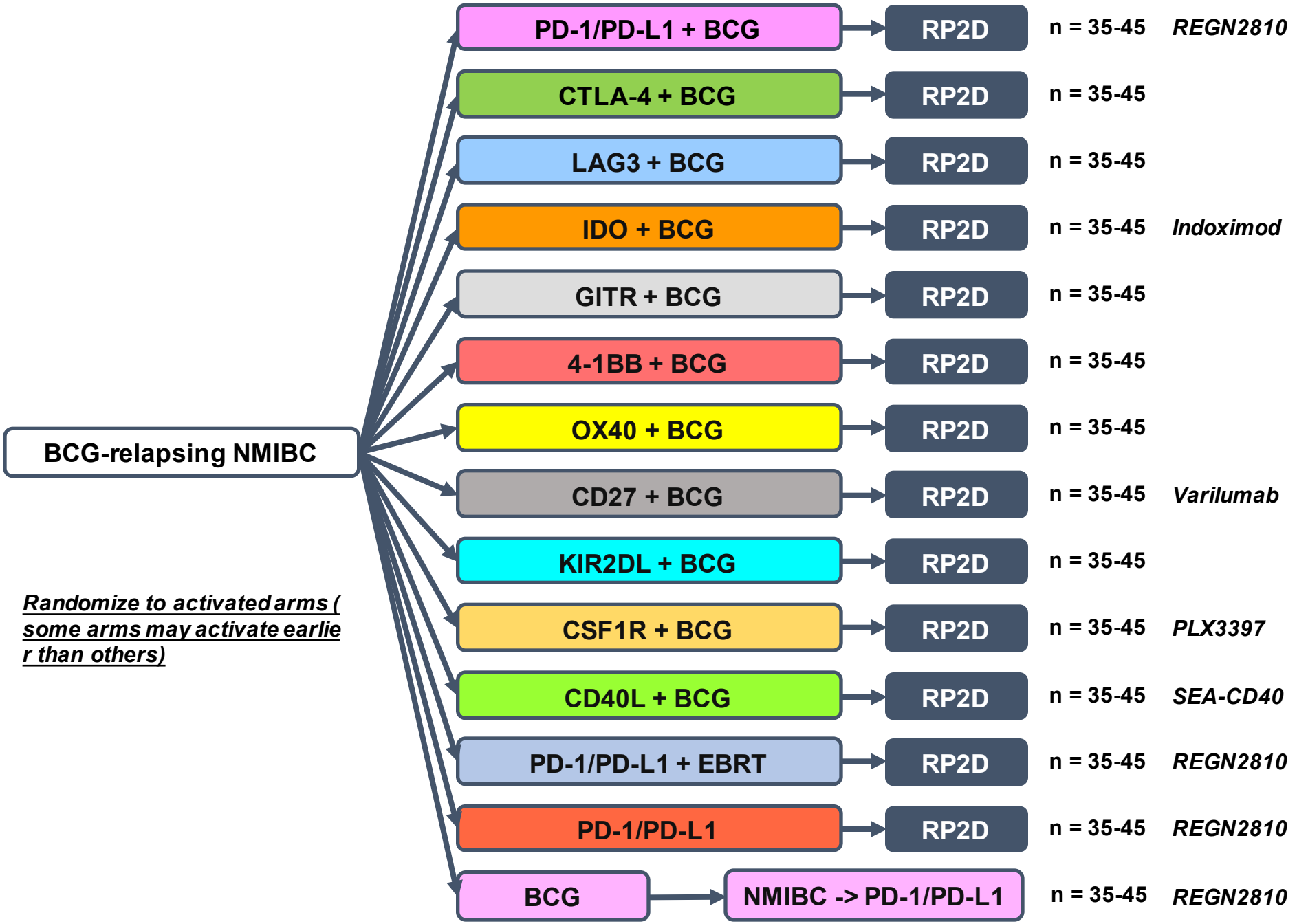
- Dual checkpoint inhibition
  - Anti-PD-1/PD-L1 + Anti-CTLA-4
  - INCB24360, Indoximod (IDO1)
  - BMS-986016 (LAG3)
  - MGA271 (B7-H3)
- Checkpoint + costim Rc
  - Varlilumab (CD27)
  - Urelumab, PF-05082566 (4-1BB)
  - MEDI6469 (OX40)
  - MK-4166 (GITR)
- Checkpoint + Radiation
  - EBRT, SBRT
- Checkpoint + chemoRx
- Checkpoint + NK-cell
  - ALT-803 (IL-15), Lirilumab (Anti-KIR)
- Checkpoint + Epigenetic agents
  - Demethylating agents: 5-azacitidine
  - HDACi: Entinostat, Vorinostat
- Checkpoint + Vaccine
  - GVAX, Sipuleucel-T, ProstVac, pTVG-HP
- Checkpoint + Cytokines
  - IL-2, IFN
- Vaccine + Cytokine
  - modified gp100 peptide + IL-2
  - ProstVac + GM-CSF
- Checkpoint + TKIs
  - VEGF
  - BTK (Ibrutunib, ACT-196)

# Selective Ongoing Combination Immunotherapy Trials in GU Cancers

| Agent | Clinical Trial Design | Phase | Identifier |
|---|---|---|---|
| **PROSTATE** | | | |
| Sipuleucel-T | Sipuleucel-T with concurrent vs. sequential AA | Randomized PII | NCT01487863 |
| | Sipuleucel-T with concurrent vs. sequential Enz | Randomized PII | NCT01981122 |
| | Sipuleucel-T ± Radium-223 | Randomized PII | NCT02463799 |
| | Sipuleucel-T ± RT | Randomized PII | NCT01807065 |
| | Sipuleucel-T with immediate vs. delayed ipilimumab | Randomized PII | NCT01804465 |
| Prostvac-VF | Rrostvac-VF ± GM-CSF vs. placebo | Randomized PIII | NCT01322490 |
| | Enz ± Rrostvac-VF | Radomized PII | NCT01867333 |
| | Docetaxel ± Prostvac-VF | Radomized PII | NCT01145508 |
| Ipilimumab | Ipilimumab + AA | Single-arm PII | NCT01688492 |
| | Ipilimumab + ADT | Single-arm PII | NCT01498978 |
| Pembrolizumab | Pembrolizumab + pTVG-HP | PI/II | NCT02499835 |
| | ADXS-PSA +/- Pembrolizumab | PI/II | NCT02325557 |
| **RENAL CELL CARCINOMA** | | | |
| Nivolumab/ Ipilimumab | Nivolumab + Ipilimumab vs. sunitinib | Randomized PIII | NCT02231749 |
| | Nivolumab + Bevacizumab vs. Ipilimumab | Randomized PII | NCT02210117 |
| MPDL3280A | MPDL3280A + Bevacizumab vs. sunitinib | Randomized PIII | NCT02420821 |
| Pembrolizumab | Pembrolizumab ± Pazopanib | PI/II | NCT02014636 |
| | Pembrolizumab ± Pazopanib | PI | NCT02133742 |
| | Pembrolizumab + PegIFN-2b vs. Pembrolizumab + Ipilimumab | PI/II | NCT02089685 |
| | Pembrolizumab + Bevacizumab | PI/II | NCT02348008 |
| | Pembrolizumab + INCB024360 | PI/II | NCT02178722 |
| DC-vaccine | DC-vaccine + Cytokine-Induced Killer Cell vs. IL-2 | Randomized PII | NCT00862303 |
| HD IL-2 | HD IL-2 + entinostat | PI/II | NCT01038778 |
| | HD IL-2 + Radiation | Single-arm PII | NCT01884961 |
| | HD IL-2 + SBRT | Single-arm PII | NCT02306954 |
| **UROTHELIAL CARCINOMA** | | | |
| Nivolumab | Cabozantinib + Nivolumab ± Ipilimumab | PI | NCT02496208 |
| Pembrolizumab | Pembrolizumab + Docetaxel or Gemcitabine | PI | NCT02437370 |
| | Pembrolizumab + INCB024360 | PI/II | NCT02178722 |
| | Pembrolizumab + Gemcitabine (Neoadjuvant) | PI/II | NCT02365766 |
| | Pembrolizumab + ACT-196 | Randomized PII | NCT02351739 |

# Mix & Match? Shotgun?

- Biologic rationale
- Clinically unmet need
- Biomarker
- Novel trial design


BCG-relapsing NMIBC
Randomize to activated arms ( some arms may activate earlie r than others)
PD-1/PD-L1 + BCG
RP2D
n = 35-45
REGN2810
CTLA-4 + BCG
RP2D
n = 35-45
LAG3 + BCG
RP2D
n = 35-45
IDO + BCG
RP2D
n = 35-45
Indoximod
GITR + BCG
RP2D
n = 35-45
4-1BB + BCG
RP2D
n = 35-45
OX40 + BCG
RP2D
n = 35-45
CD27 + BCG
RP2D
n = 35-45
Varilumab
KIR2DL + BCG
RP2D
n = 35-45
CSF1R + BCG
RP2D
n = 35-45
PLX3397
CD40L + BCG
RP2D
n = 35-45
SEA-CD40
PD-1/PD-L1 + EBRT
RP2D
n = 35-45
REGN2810
PD-1/PD-L1
RP2D
n = 35-45
REGN2810
BCG
NMIBC -> PD-1/PD-L1
n = 35-45
REGN2810

# Conclusions/Future Directions

- The promising data of cancer vaccine and checkpoint inhibitors have opened new frontiers in IT for cancer
- Limitations exist with current IT such as low response rate and lack of reliable biomarkers
- Combinational approach is expected to overcome current limitations and maximize the benefit of IT
- New IT trials with sold biologic rationale and novel trial designs in clinically unmet need population are warranted


Cancer
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2020