



Immunotherapy's Coming Of Age As An Effective Modality For Cancer Treatment

Robert H. Wiltout, Director, SD for Basic Science

Lee J. Helman, SD for Clinical Research

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CENTER FOR CANCER RESEARCH



Science

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Breakthrough of the Year

Cancer Immunotherapy

T cells on the attack



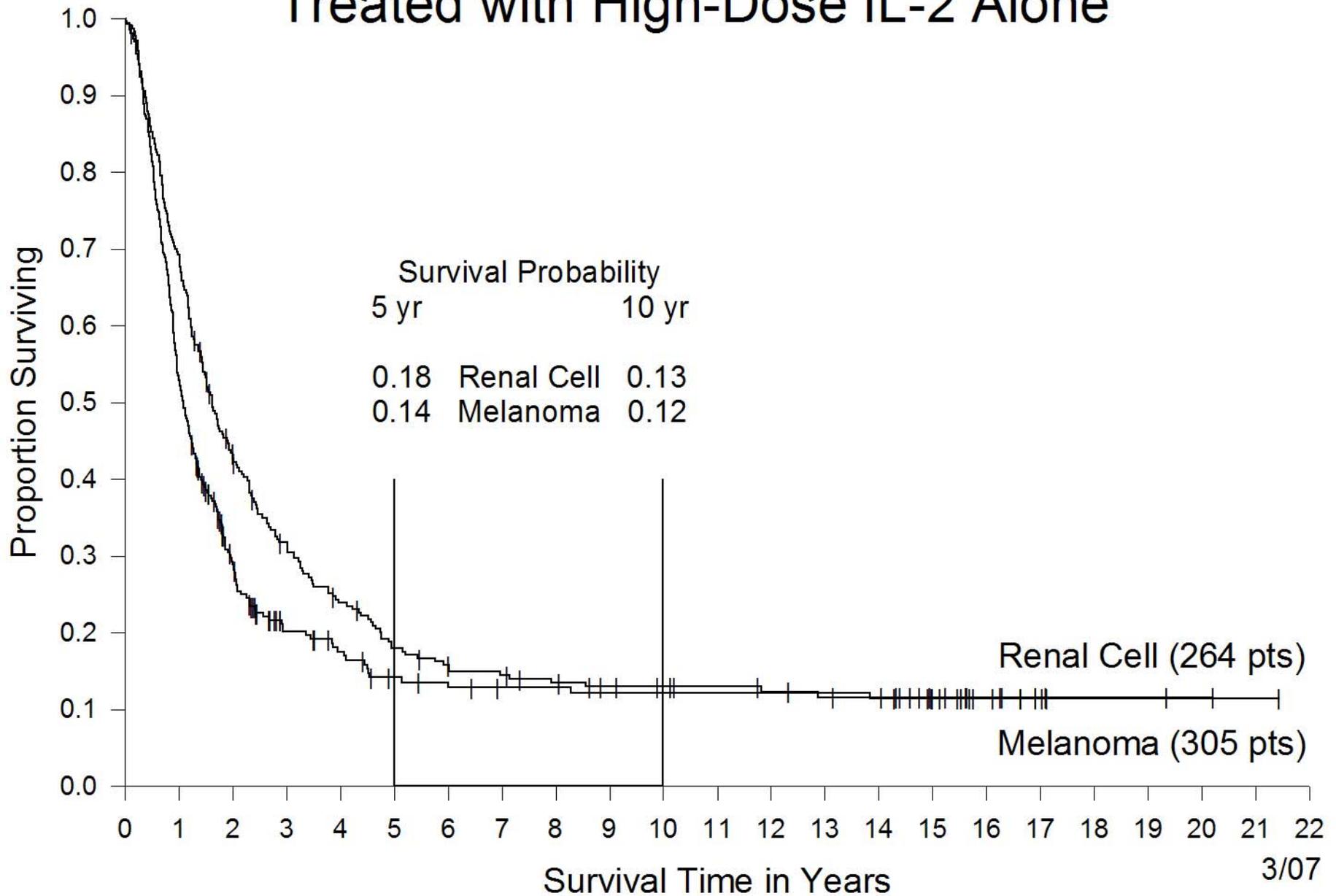
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Immunotherapy's Coming Of Age As An Effective Modality For Cancer Treatment

- Reports of clinical responses increasing in frequency and across disease types, including for cancers previously thought to be refractory to immunotherapy
 - **B cell lymphomas, sarcomas, lung, pancreatic, ovarian etc.**
- Consistent reports of plateaus (long tails) in survival curves
 - Cytokines, checkpoint inhibitors, chimeric antigen receptors, adoptively transferred cells
- A low frequency of durable responses contrasts with results for many molecularly targeted agents which may induce a higher frequency of short duration responses
- Can we develop better ways to strategically combine molecularly targeted agents with immunotherapy?
- Can a better understanding of durable immune-induced responses provide better insight into overall development of cancer therapeutics?

569 Patients with Metastatic Disease Treated with High-Dose IL-2 Alone



More focused strategies to exploit adaptive/antigen-specific immunity

Adoptive Transfer

**Cellular-targeted modulation of tumor immunity:
reinfused patient-autologous T cells manipulated ex vivo**

- transduction to express Ab to chimeric antigen receptors (aCD19, aCD20)
- expansion of tumor-infiltrating lymphocytes (TILs)

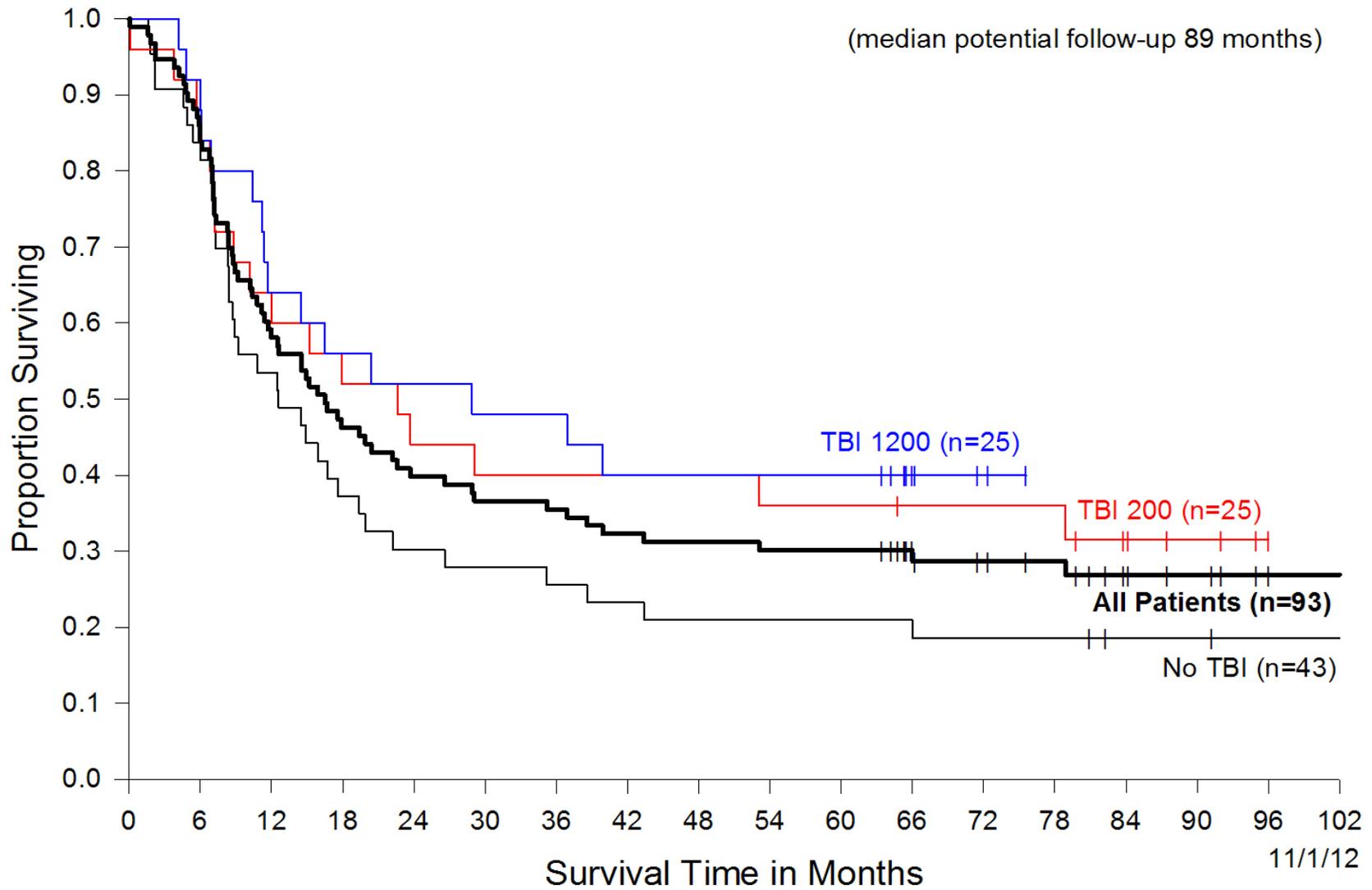
Targeted effects through checkpoints and costimulatory molecules

Molecule-targeted antibody-based modulation of tumor immunity

- aCTLA4 (ipilimumab)
- aPD-1 (nivolumab, lambrolizumab, pidilizumab, AMP-224)
- aPD-L1 (MPDL3280A, MEDI-4736)
- α CD40

Survival of Patients with Metastatic Melanoma Treated with Autologous Tumor Infiltrating Lymphocytes and IL-2

(median potential follow-up 89 months)

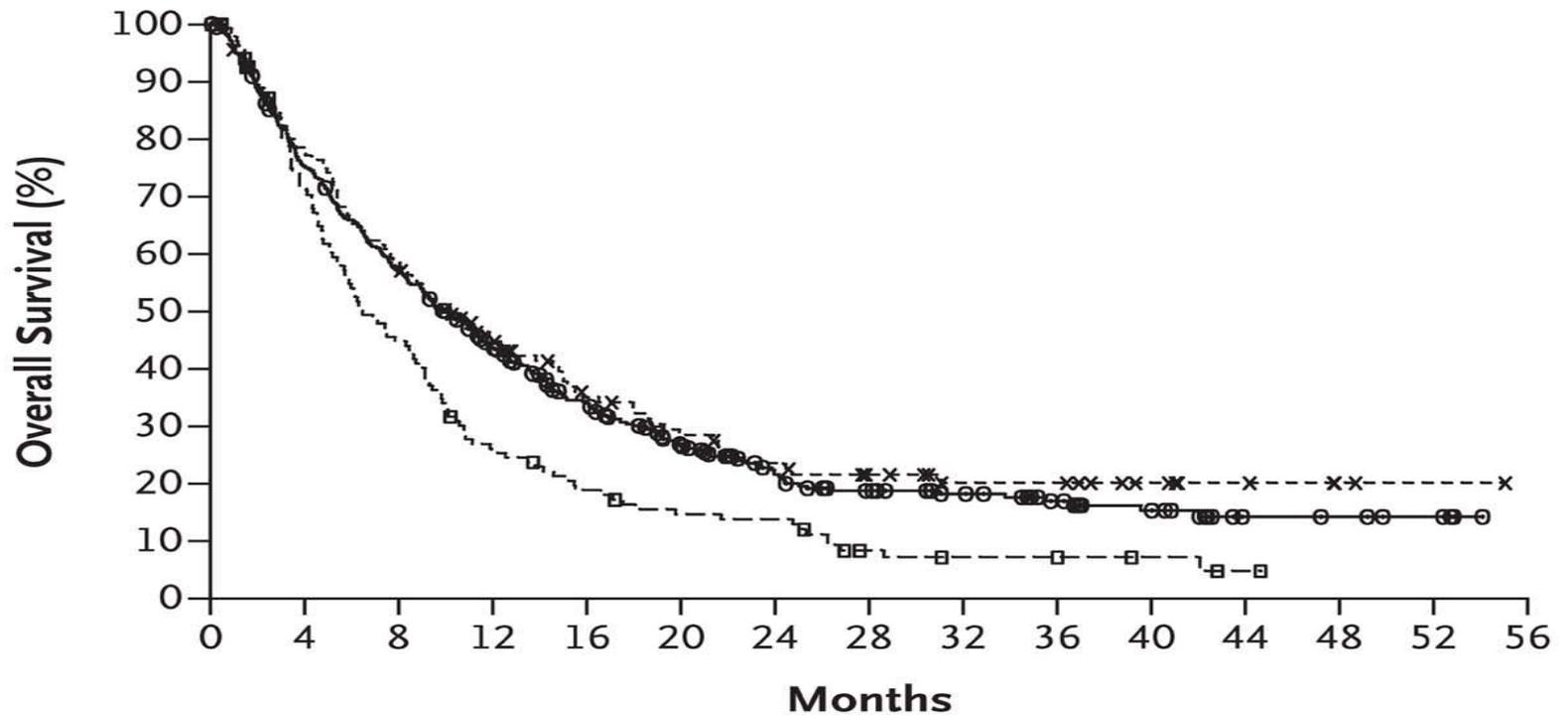


Checkpoint inhibitors: Anti-CTLA4 as a guide



— Ipi plus gp100 - - - - Ipi - - - - gp100
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A Overall Survival



No. at Risk

Ipi plus gp100	403	297	223	163	115	81	54	42	33	24	17	7	6	4	0
Ipi	137	106	79	56	38	30	24	18	13	13	8	5	2	1	0
gp100	136	93	58	32	23	17	16	7	5	5	3	1	0	0	0



While we work forward in developing molecularly targeted agents based on genomic anomalies in human cancers...

Should we not also work backward to understand how the more frequent and durable responses now being seen with immunotherapy might accelerate the overall approach to cancer treatment?

