Demonstrating the Impact of MRA-funded Research: A Case Study

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Melanoma Research Alliance

Mission

This mission of the Melanoma Research Alliance is to end suffering and death due to melanoma by collaborating with all stakeholders to accelerate powerful research, advance cures for all patients, and prevent more melanomas

MRA Grant Portfolio Overview

312 Awards Granted

$111 Million Invested

144 Institutions

18 Countries

MRA Grant Solicitation and Selection Process

- **Release Annual Request for Proposals (RFP)** – includes Special Emphasis Areas, Special Opportunities

- **Grants Reviewed by standing Grant Review Committee:**
  - Online triage step
  - In-person Grant Review Committee meeting

- **Slate of grants approved by MRA Board of Directors**

MRA Grant Award Mechanisms

Team Research: requires multidisciplinary teams and involvement of a Young Investigator. $900k and up over 3-years

Established Investigator: past their first four years of appointment with an established record of scientific productivity. $375k over 3-years

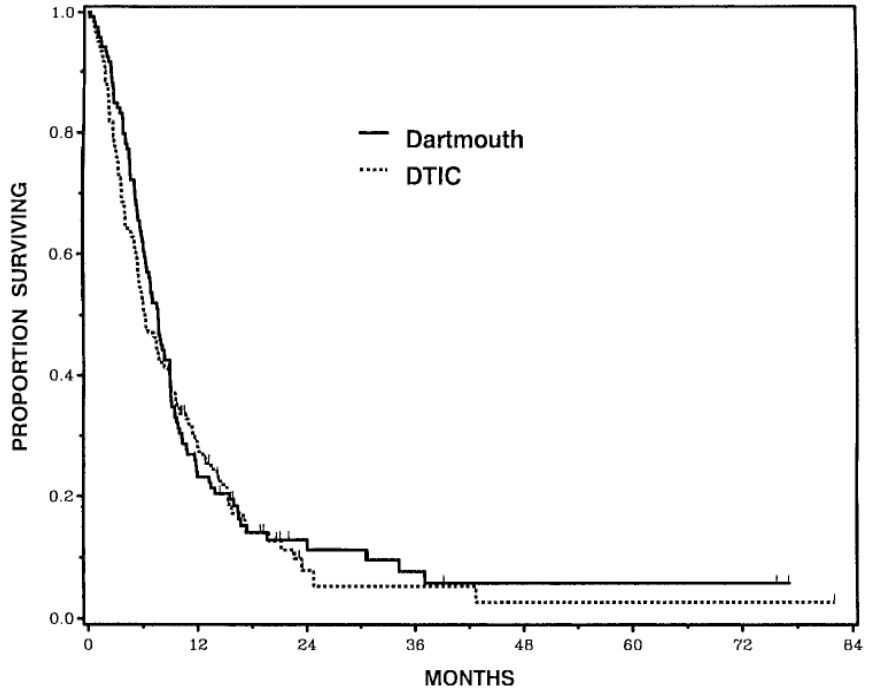
Young Investigator: within four years of first faculty appointment, requires a mentorship commitment from a senior investigator. $225k over 3-years

Pilot: test potentially transformative ideas that may not have extensive data, but articulate a clear hypothesis – “high-risk, high-reward.” $100k over 2-years

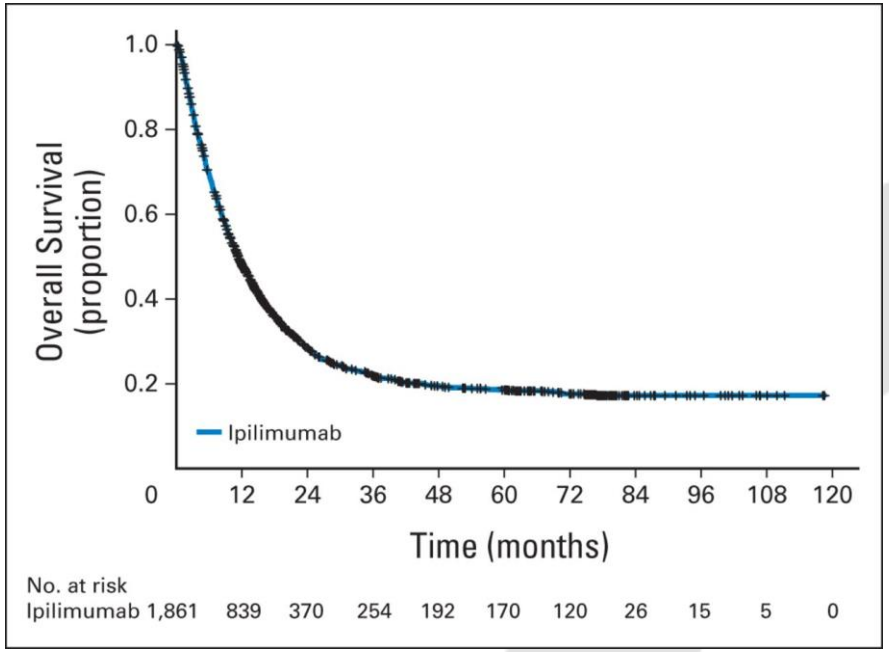
Dermatology Fellow: engaging clinical dermatologists in melanoma research, requires mentorship and fellowship in Dermatology Department. $35k for 1-year; year 2 possible

How do we assess MRA's multi-million dollar investment in melanoma research?

Patient outcomes have changed dramatically since MRA's founding

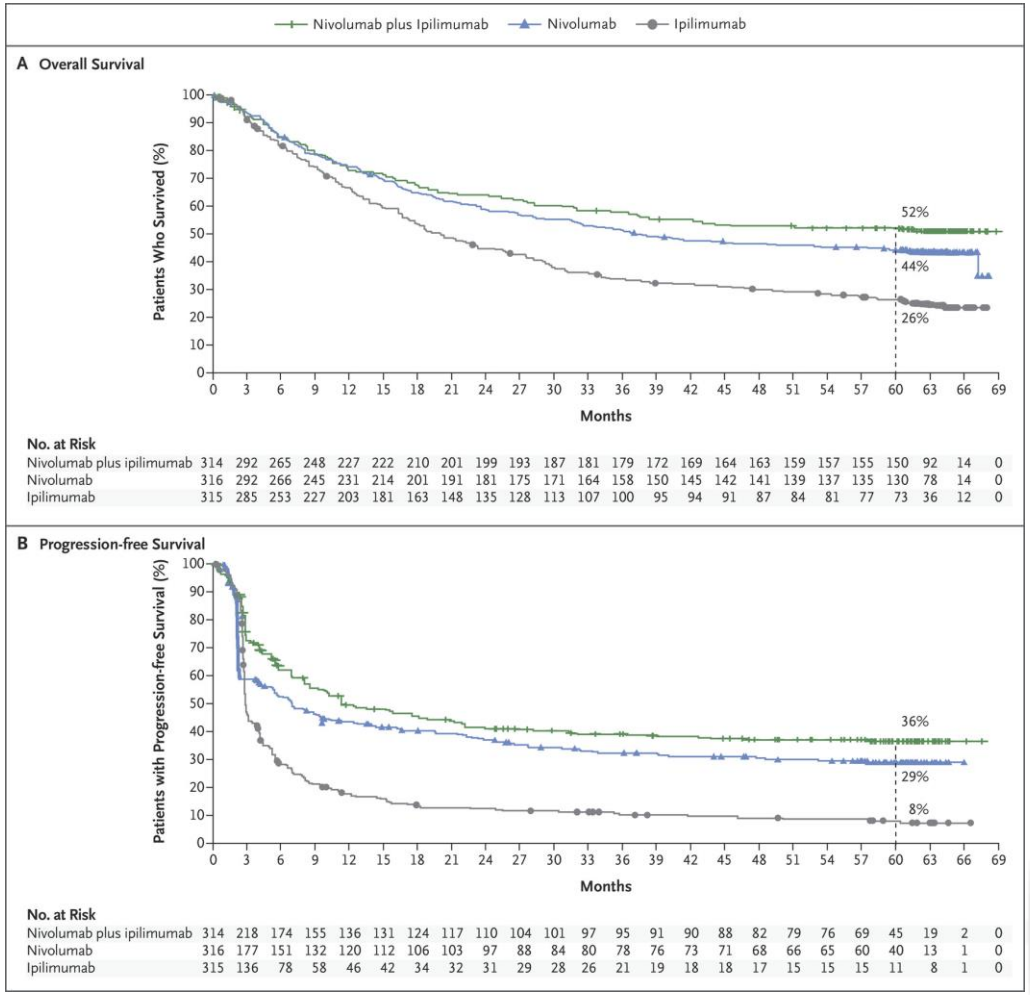


Chapman et al. J Clin Oncol, 1999



Schadendorf et al. JCO 2015;33:1889-1894

5-year survival >50%, 12 new treatments approved



Larkin et al. N Engl J Med 2019

IMPACT 2018: Methodology

- **IMPACT 2015:** Evaluated progress towards Scientific Aims for the first 63 completed awards from MRA's portfolio in 2015-2016.

- **IMPACT 2018:** Took a 3-pronged approach:

    1. Evaluated progress towards Scientific Aims for the projects completed after IMPACT 2015 and before 2017 (44 total)
    2. A post award survey was sent to the 93 admin PIs with awards evaluated as part of IMPACT 2015 and IMPACT 2018 (response rate = 74%)
        - Quantitative success measures such as follow-on funding, patents and publications
        - Feedback from funded investigators
    3. Assessment of qualitative and quantitative outcomes for 107 awards evaluated as part of IMPACT 2015 and IMPACT 2018
        - Used combination of data from Progress Reports, Dimensions, PubMed, www.uspto.gov, Post Award Survey

Together, IMPACT 2018 allowed us to:

- Highlight key results from MRA's research funding on melanoma and cancer; and,
- Develop lessons learned and opportunities for improvement.

IMPACT 2018: Presenting the Results

Results from IMPACT 2018 were presented to the MRA Board in November, 2018

The full report included:

1. Executive Summary
2. PowerPoint presentation of key summary data
3. Key Award Examples
4. Detailed 17 page report
5. Individual 1-2 pg project summaries for each award assessed

The results were also presented publicly at the international conference *AACR Melanoma: Biology to Target* and 2019 MRA Scientific Retreat

IMPACT 2018: Outcomes Summary

Award Mechanisms	Number of Awards	Amount Funded	Amount of Follow-on Funding	ROI (Additional Funding/Award Funding)	Number of Patent Applications	Number of Patents Awarded	Number of Publications	Number of Presentations	Number of Collaborations
Pilot	13	$1.1M	$5.2M	4.7	4	2	26	23	26
Established Investigator	31	$7.5M	$51.4M	6.8	10	4	136	332	77
Team Science	32	$27.4M	$70.8M	2.6	26	16	212	306	123
Young Investigator	28	$4.8M	$26M	5.4	10	6	127	152	77
Total	**107**	**$42.7M**	**$153.6M**	**3.6**	**50**	**28**	**543**	**827**	**307**

IMPACT 2018: High Impact Publications

Award Mechanism	Title	Year	Journal	Citations
Young Investigator	Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients	2017	Nature Medicine	139
Pilot	Phosphoenolpyruvate Is a Metabolic Checkpoint of Anti-tumor T cell Responses	2015	Cell	250
Team Science	Commensal Bifidobacterium promotes antitumor immunity and facilitates anti–PD-L1 efficacy	2015	Science	487
Team Science	Melanoma-intrinsic β-catenin signalling prevents anti-tumour immunity	2015	Nature	458
Established Investigator	The Genetic Landscape of Clinical Resistance to RAF Inhibition in Metastatic Melanoma	2014	Cancer Discovery	376
Established Investigator	Highly Recurrent TERT Promoter Mutations in Human Melanoma	2013	Science	782
Young Investigator	Immunologic correlates of the abscopal effect in a patient with melanoma	2012	New England Journal of Medicine	881
Established Investigator	Modelling vemurafenib resistance in melanoma reveals a strategy to forestalldru g resistance	2013	Nature	363
Young Investigator	Radiation and dual checkpoint blockade activate non-redundant immune mechanisms in cancer	2015	Nature	592
Young Investigator	Evaluating cell lines as tumour models by comparison of genomic profiles	2013	Nature Communications	418
Team Science	Tumour exosome integrins determine organotropic metastasis	2015	Nature	775

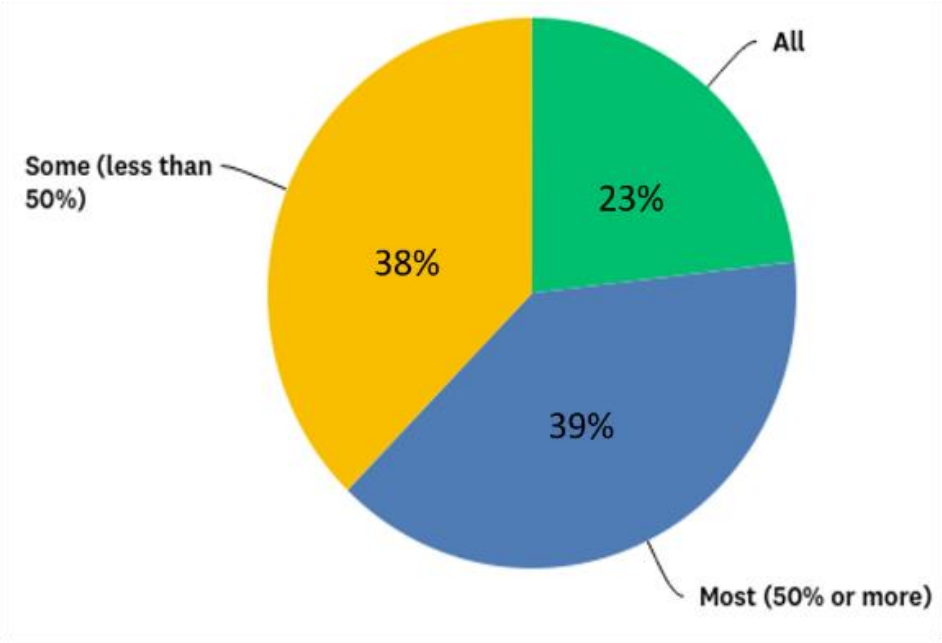
IMPACT 2018: Respondents Ranked List of Impact of MRA Awards on Career and Research Trajectory

Areas of highest impact
Expanding an existing collaboration
Establishing a new collaboration
Receiving additional funding
Using a new method or technique
Expanding the lab

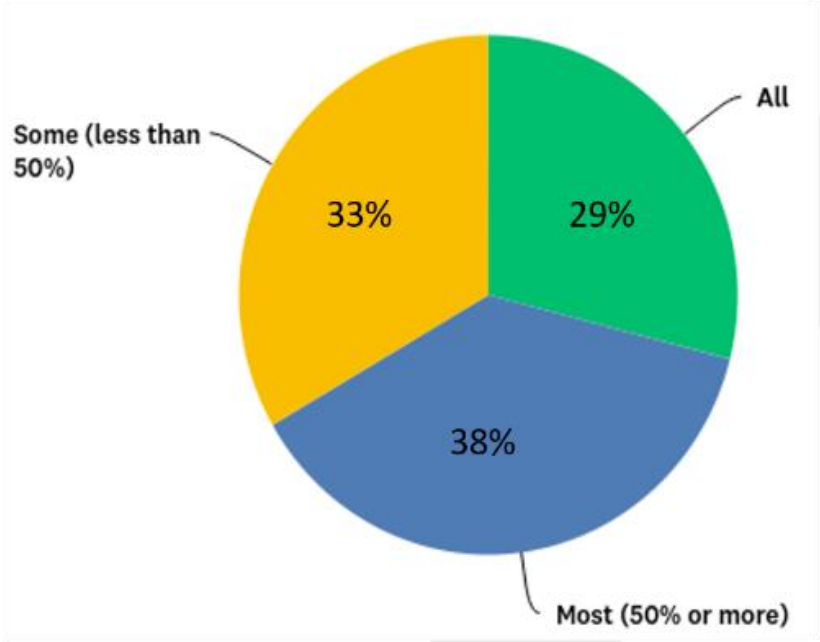
Areas of least impact
Applying for or receiving a patent
Transitioning from clinical to basic research
Starting a biotech company

IMPACT 2018:
Proportion of Lab Focused on Melanoma Research

Proportion focused on melanoma prior to receiving award



Proportion currently focused on melanoma



IMPACT 2018: Key Examples/Award Summaries

TITLE	Publications 20 Presentations 27 Patent applications 2 Clinical trials 2 Collaborations 6 Follow-on grants 6 Follow-on funding $4,260,000
TEAM MEMBERS AND INSTIUTION	
Team Science Award (TSA)	
7/1/2013 – 6/30/2016 Budget Proposed: $1,000,000 **Budget Actual: $900,000** Budget Notes: Budget reduction	
Status: 2 years post completion	

Progress Summary

Immunotherapy, especially strategies to enable the immune system to overcome immune checkpoint inhibition, provide remarkable benefit, but only in a subset of melanoma patients. Clinical responsiveness to immune checkpoint inhibitors may depend on if the patient has tumors with spontaneously occurring inflammatory features and a pre-existing immune response at the tumor sites. This project used patient samples, existing data in TCGA (The Cancer Genome Atlas), and animal models to characterize 3 mechanisms that enable this "smoldering" immune response. They identified 3 mechanisms. (i) Increased

Other Summary Components

- Aims Summary
- Progress of Scientific Aims
- List of Quantitative Metrics
- Feedback from Survey

IMPACT 2018: Key Findings

- The evolution of research topics funded by MRA reflects the progress of melanoma research as a whole over the past 11 years
- MRA funded research impacts clinical practice
- MRA funded research informs current thinking in the field
- MRA funding positively impacts the careers of funded researchers and leveraged significant dollars
- The majority of MRA's funded awards are successful, but modifications to the original aims occur, as well as technical hurdles
- Many of the conclusions drawn from IMPACT 2015 are supported by the IMPACT 2018 evaluation

IMPACT 2018: Conclusions and Recommendations

- Continue to fund a diverse range of award mechanisms
- Maintain a rigorous GRC-driven peer review process to ensure MRA awards continue to advance melanoma research and clinical practice
- Evaluate if MRA should modify its approach to funding clinical trials
- Consider expanding the number of Pilot and Young Investigator Awards MRA makes each year
- Consider broadening portfolio to fund a greater number of awards focused on prevention and diagnostics
- Evaluate the impact of the collaborative funding program, co-funding awards with other non-profits, as well as geographically-focused and topic-focused programs
- Evaluate how MRA partners with industry to fund research

IMPACT 2018: Broader Takeaways

- Significant amount of work – consultant/additional staff/dedicated staff needed
- Need staff that can go deep on the science but have a broad understanding of the field
- Important to understand needs and interests of audience
- Mix of quantitative and qualitative outcomes are often important
- Mix of platforms are necessary for the analysis if assessing program at the level of individual grants
- Organization-specific considerations: MRA is a relatively young organization, relatively small number of awards
- Field specific considerations: Melanoma research field is unique, particularly during the time period assessed in this analysis

Acknowledgements

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