

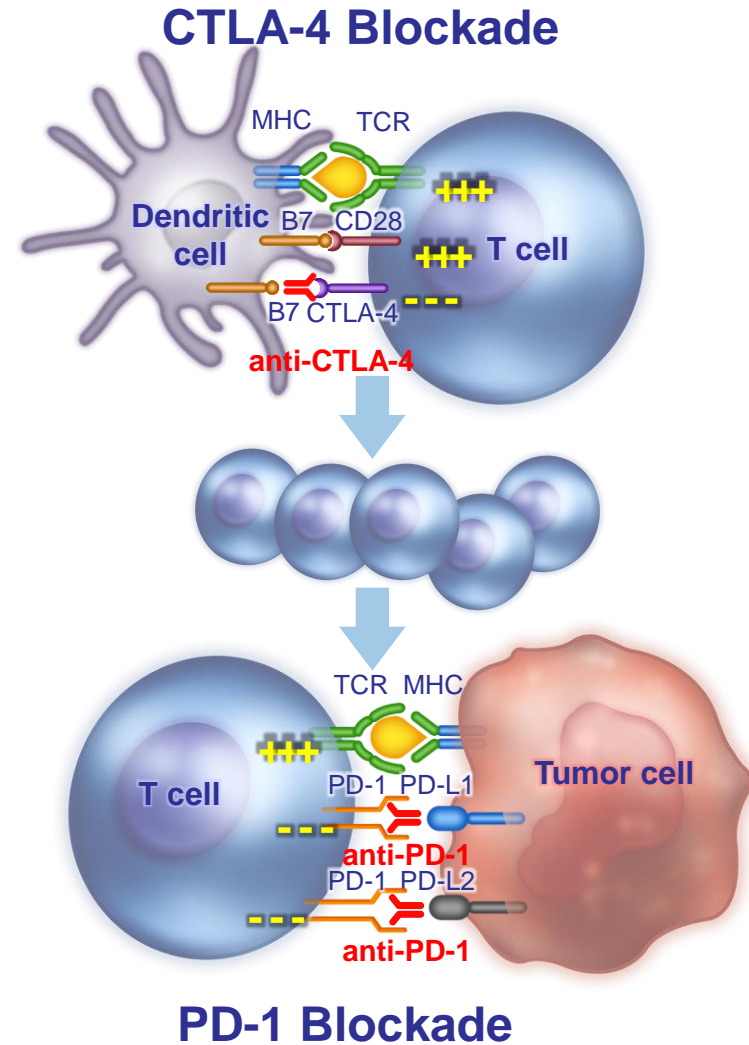
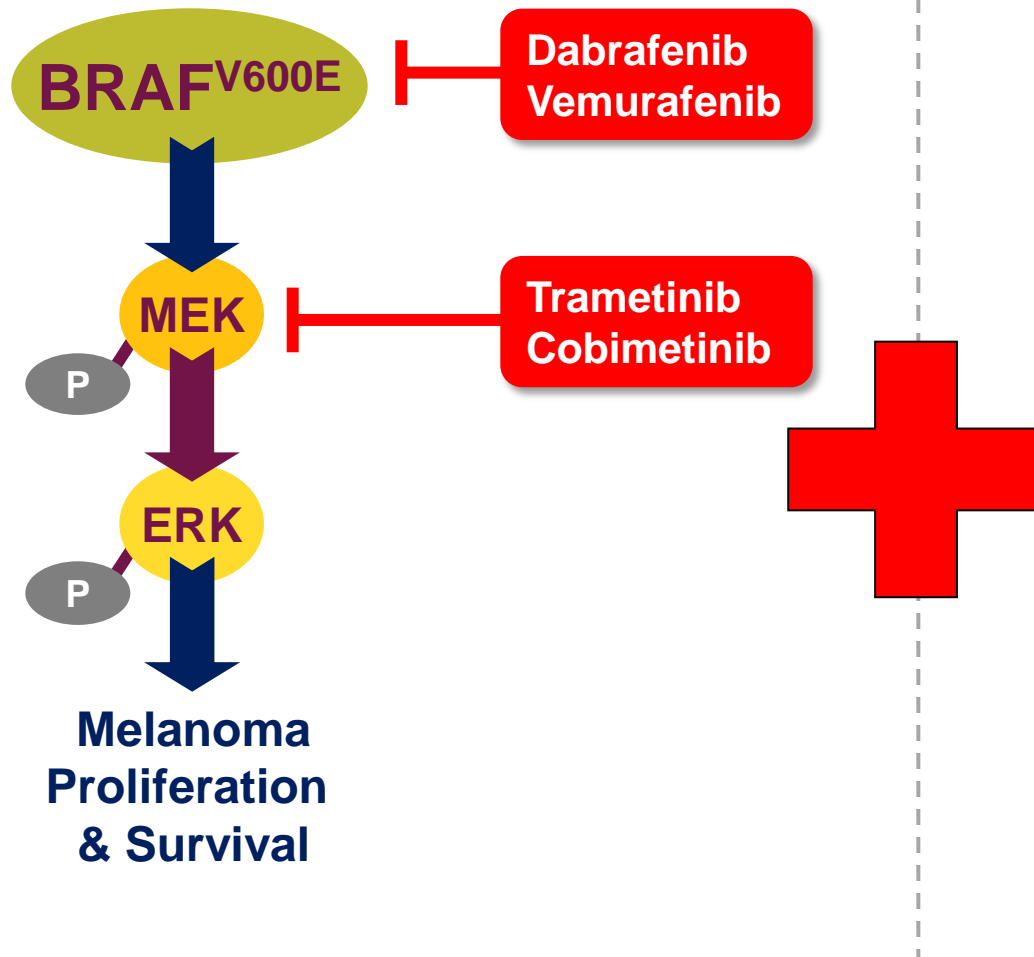
The path forward in immunotherapies- combinations: But can we afford them?

Prof Grant McArthur
Peter MacCallum Cancer Centre
University of Melbourne

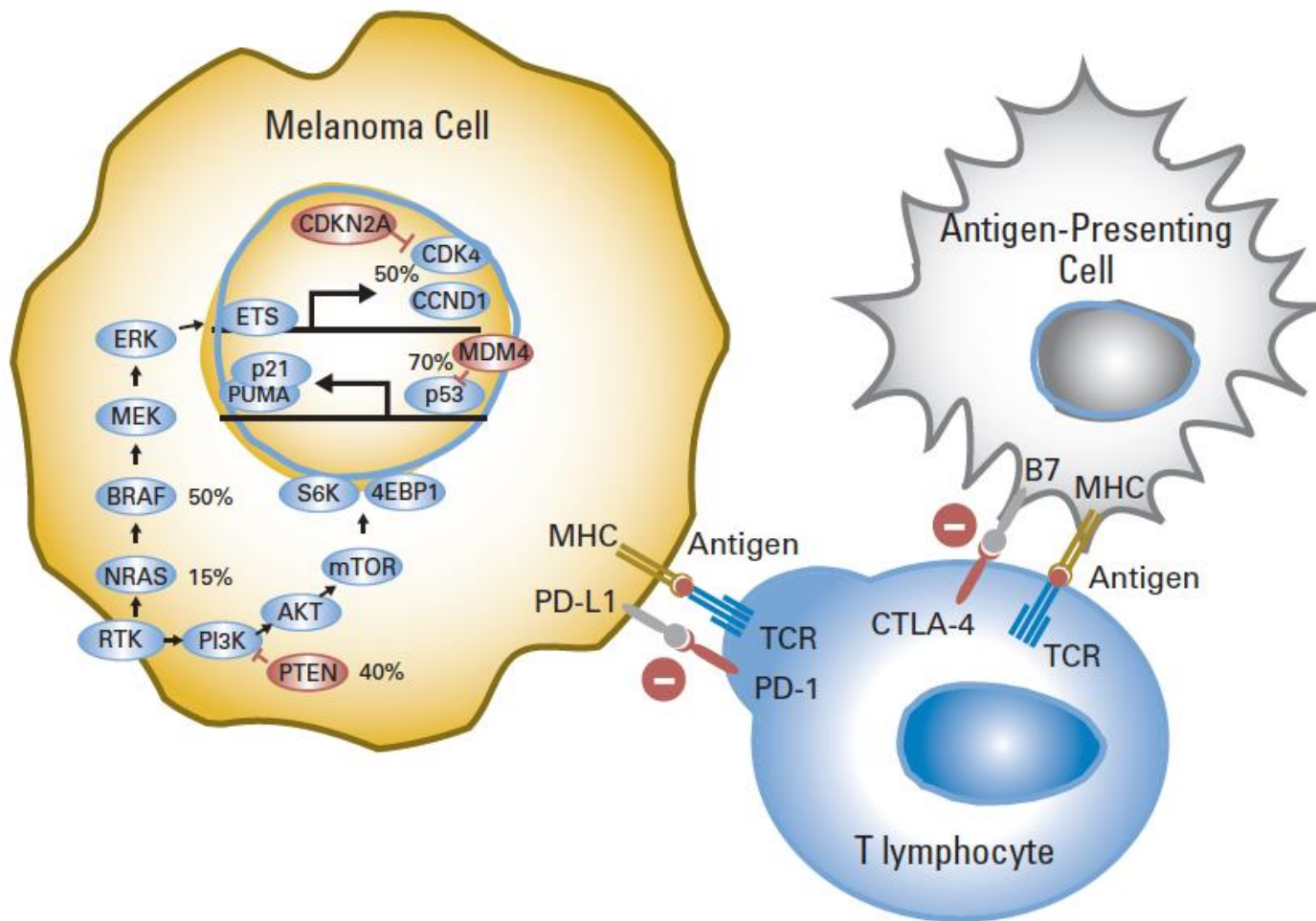
Disclosure Information

- I have the following financial relationships to disclose
 - Research support from: Pfizer, Celgene & Ventana
 - Consultant: Provectus

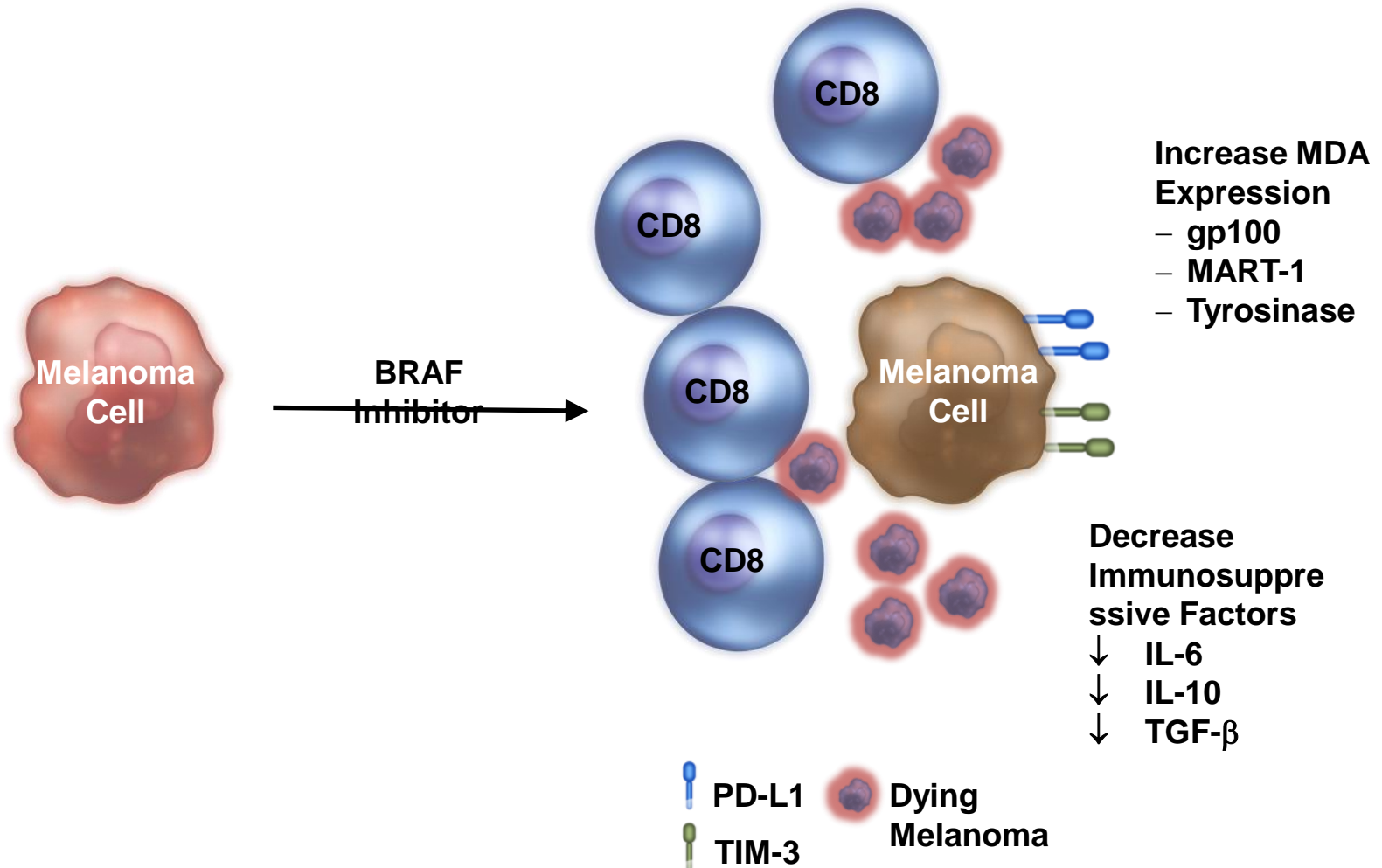
Combination approaches to treating melanoma.



Host and Tumor Cell Intrinsic Biology is Important in Cancer.



Response to BRAF-inhibition



Induction of PD-L1 Expression by the EML4-ALK Oncoprotein and Downstream Signaling Pathways in Non-Small Cell Lung Cancer

Keiichi Ota,¹ Koichi Azuma,² Eiji Iwama,¹ Taishi Harada,¹ Koichiro Matsumoto,¹ Shinzo Takamori,³ Masayoshi Kage,⁴ Tomoaki Hoshino,² Yoichi Nakanishi,¹ and Isamu Okamoto¹

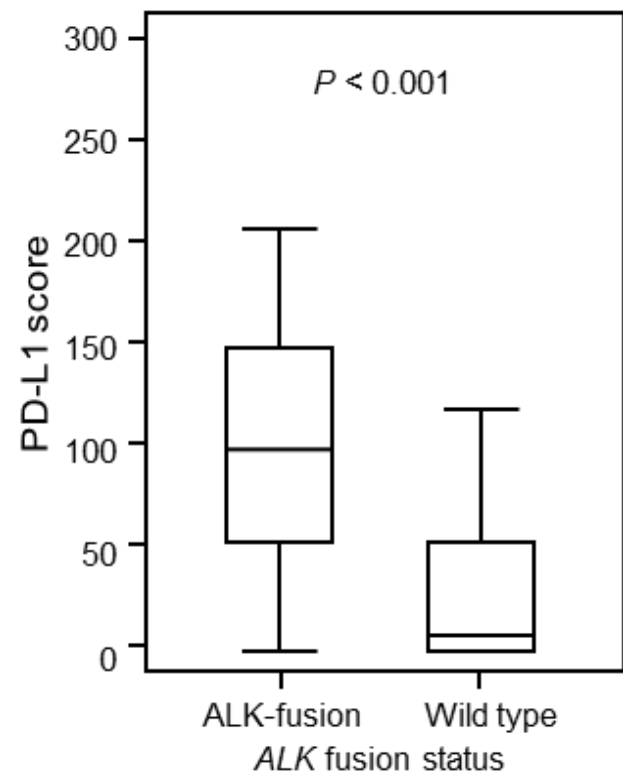
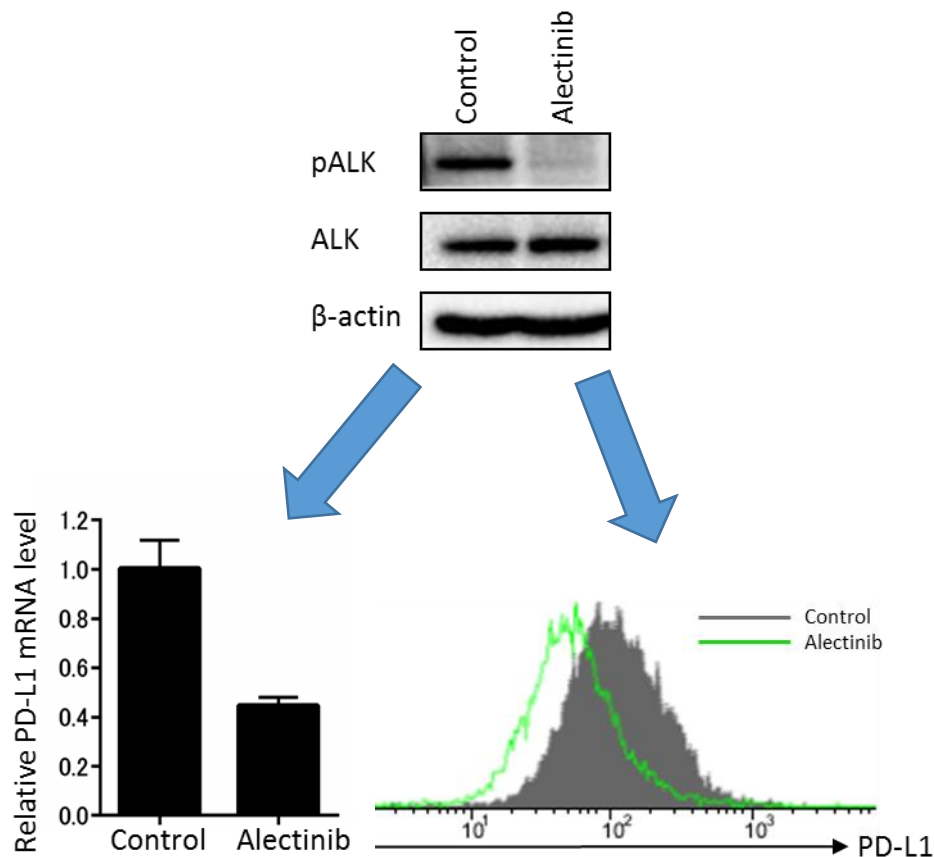
¹Research Institute for Diseases of the Chest, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan;

²Division of Respiriology, Neurology, and Rheumatology, Department of Internal Medicine, Kurume University School of Medicine, Fukuoka, Japan;

³Department of Surgery, Kurume University School of Medicine, Fukuoka, Japan;

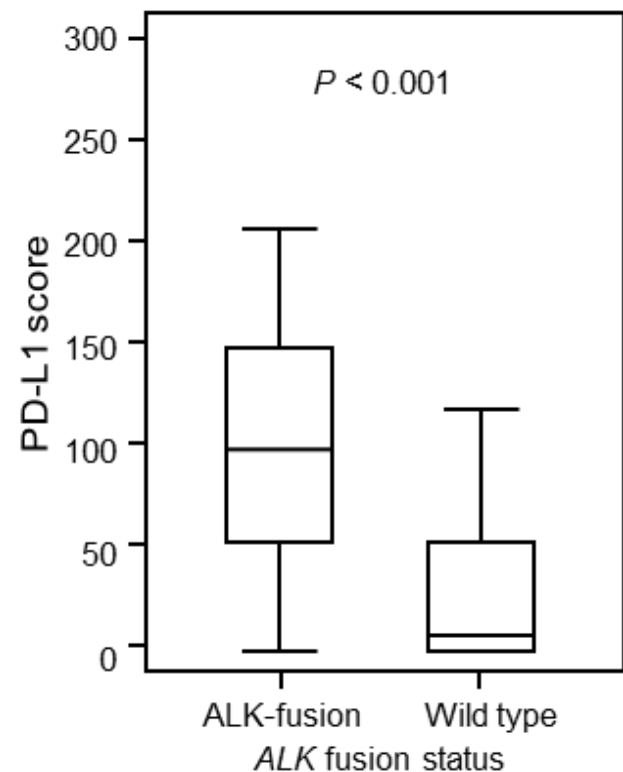
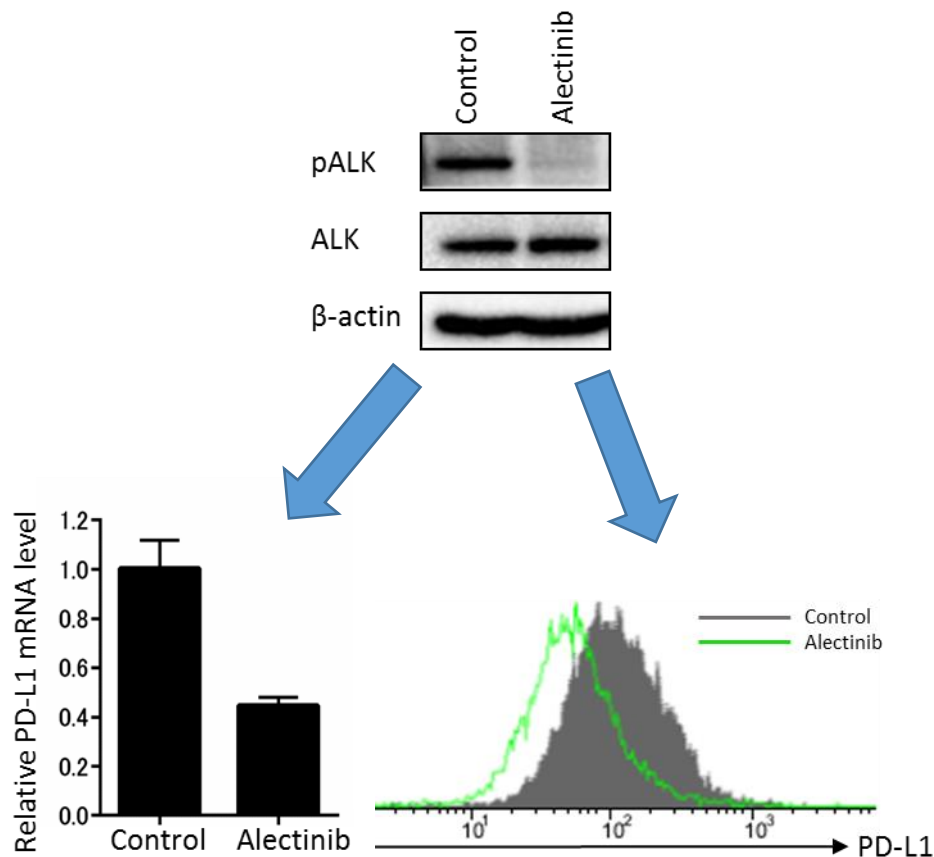
⁴Department of Diagnostic Pathology, Kurume University Hospital, Fukuoka, Japan;

Clear evidence in cell lines and patients of regulation of PD-L1 expression by EML4-ALK



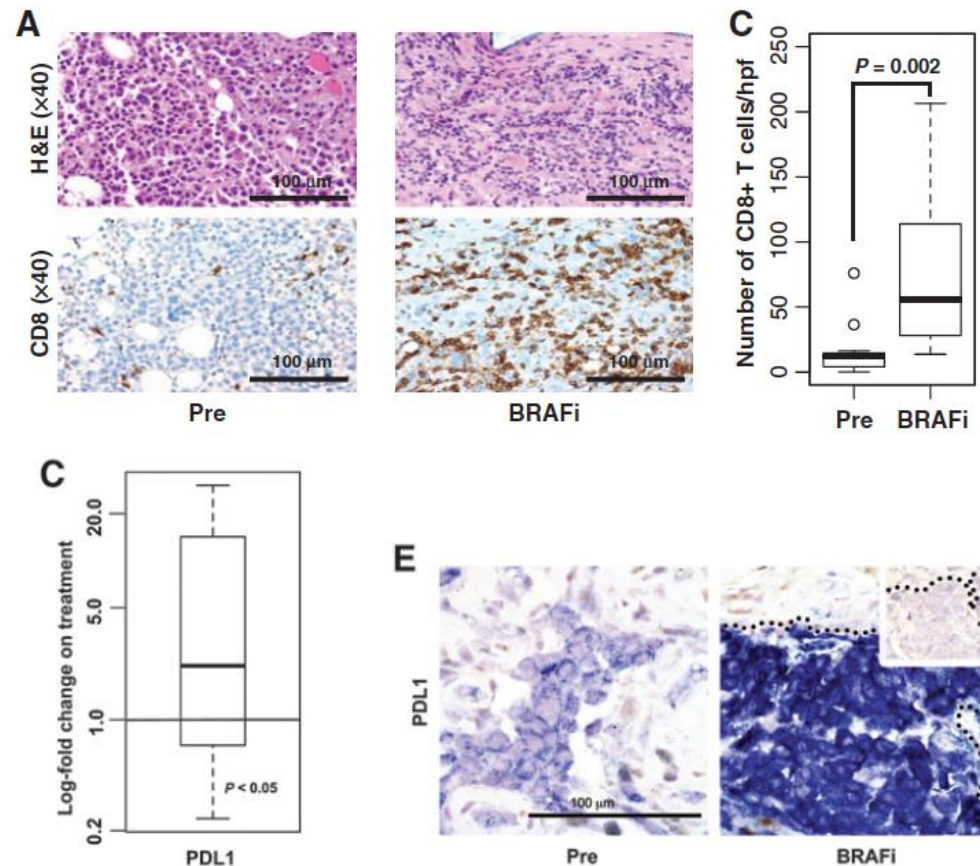
There is a need to study PD-L1 expression of EML4-ALK tumours to ALK-inhibitors in vivo in patients.

Clear evidence in cell lines and patients of regulation of PD-L1 expression by EML4-ALK



There is a need to study PD-L1 expression of EML4-ALK tumours to ALK-inhibitors in vivo in patients.

Upregulation of PD-L1 and CD8 T-cells in melanoma patients following BRAF inhibition

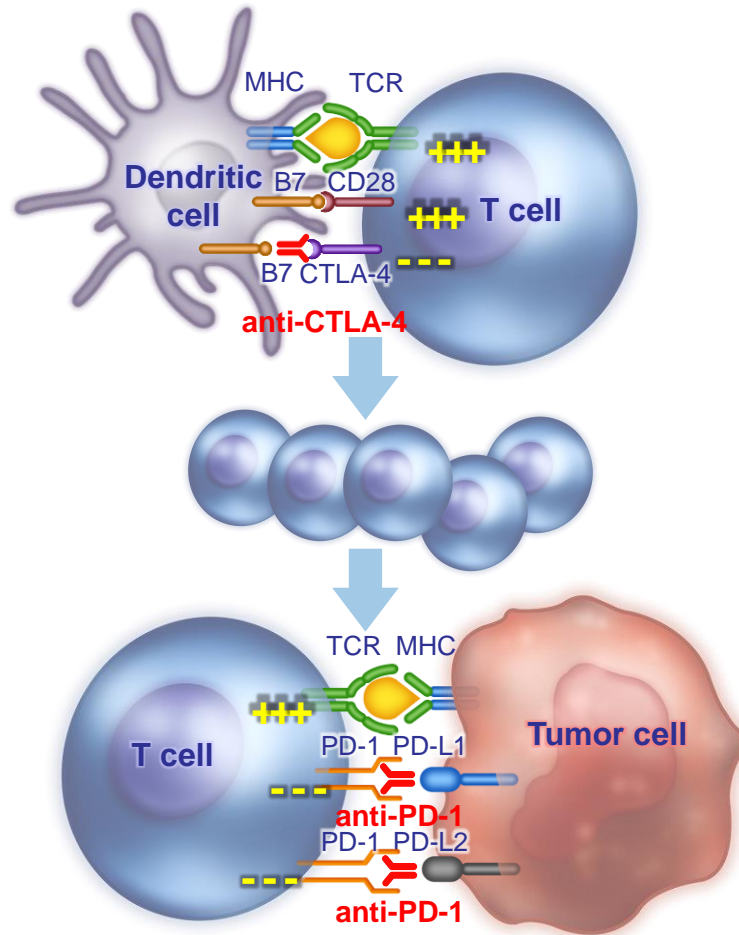


Clinical Trials of ALK and PD-1/PD-L1 inhibitors are needed

- 4 trials of BRAF/MEK inhibitors and PD-1/PD-L1 inhibitors in melanoma
 - Dabrafenib/Trametinib + Pembrolizumab
 - Dabrafenib/Trametinib + Nivolumab
 - Dabrafenib/Trametinib + MEDI4736
 - Vemurafenib/Cobimetinib + Atezolizumab

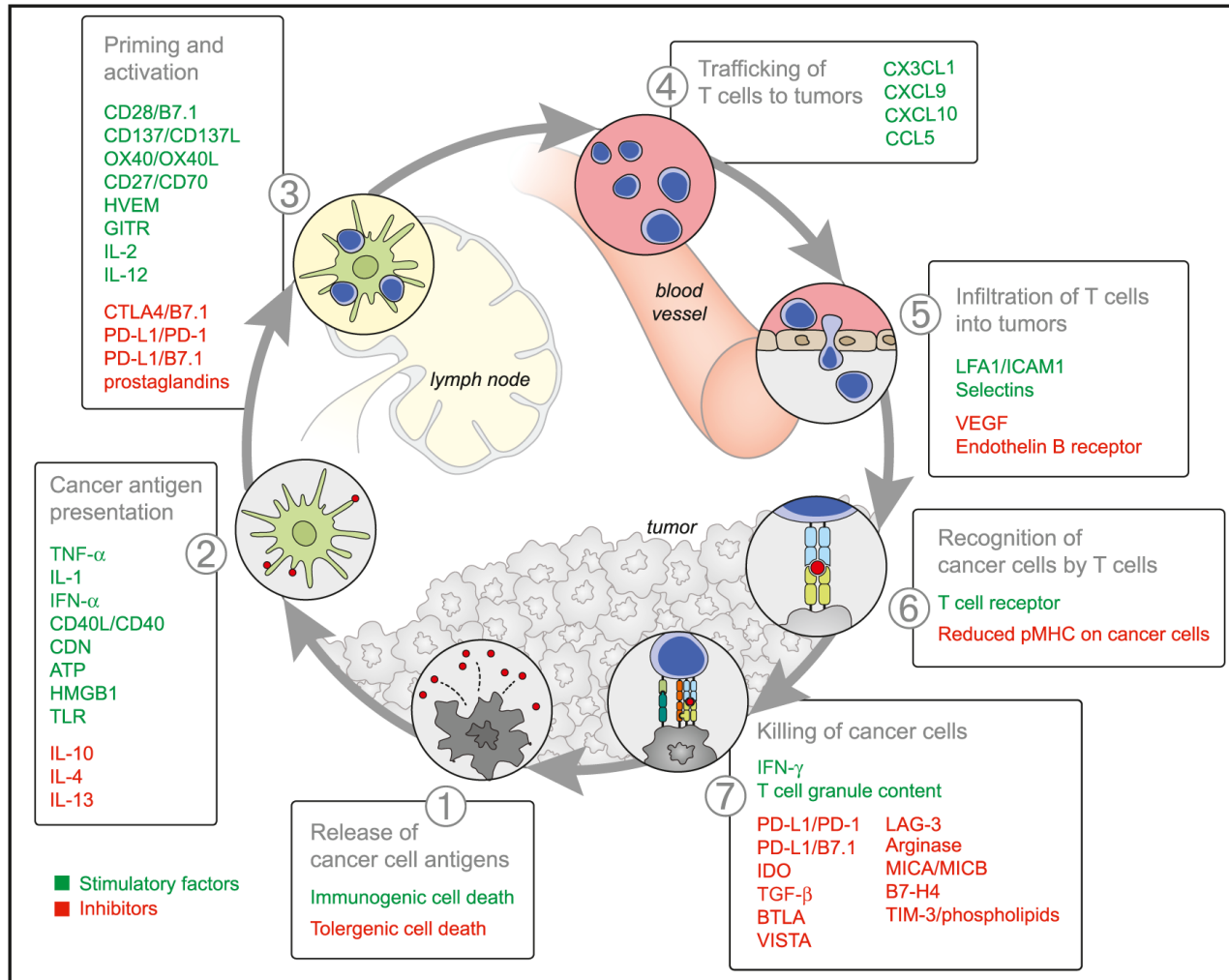
Combination approaches in immuno-oncology

CTLA-4 Blockade



PD-1 Blockade

Regulation of the Cancer-Immunity Cycle



Types of Toxicity to Oncology Drugs

Conventional toxicity

Immune-related toxicity

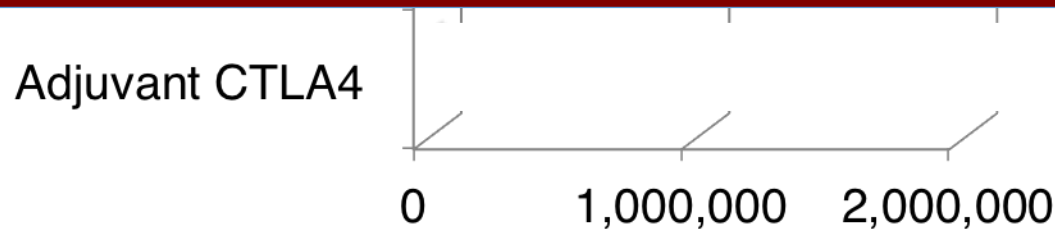
Financial toxicity!



Cost of New Melanoma Therapies in the USA - \$US

Cost of Melanoma Therapies (\$US per year)

There is strong argument to pay according to effectiveness



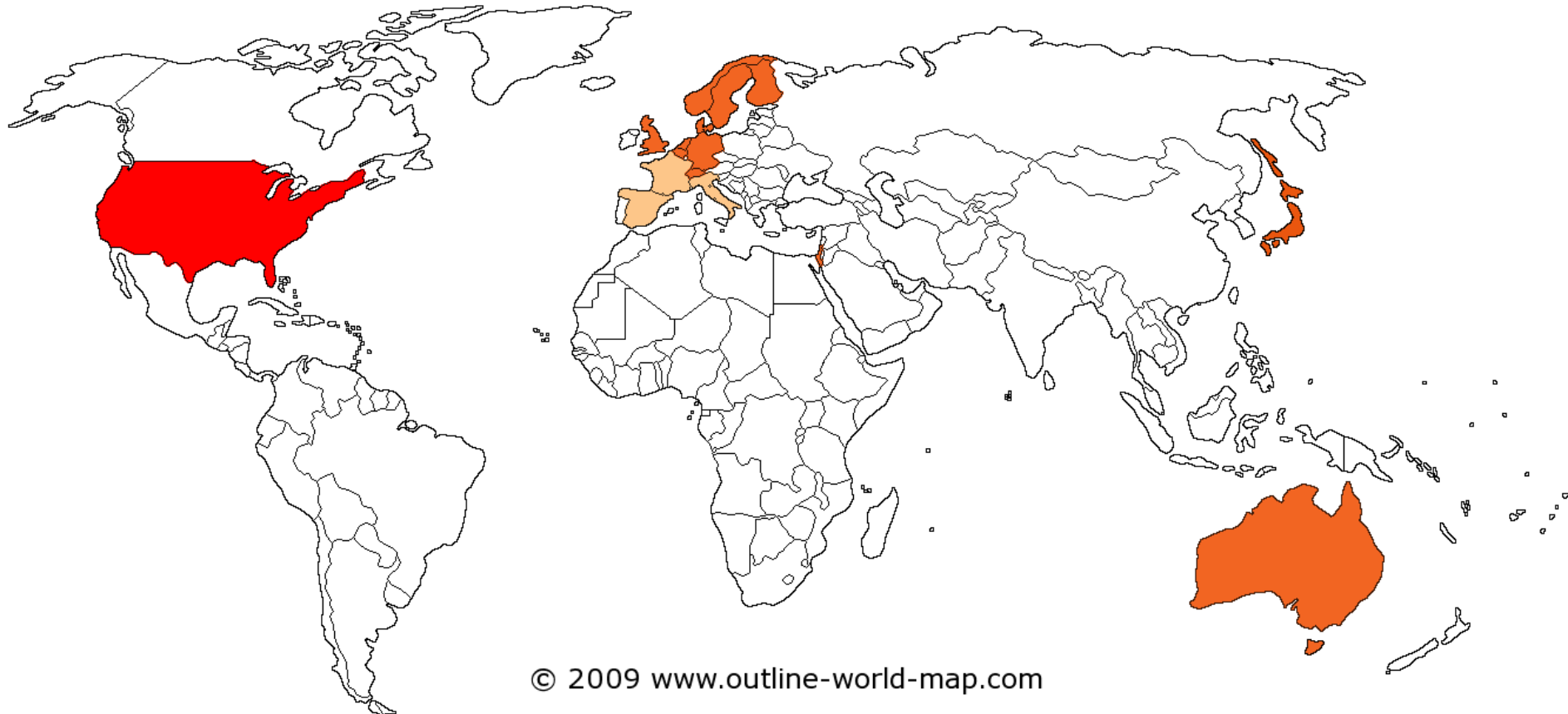
Inequities in Access to Cancer Therapies

**anti-PD-1 for melanoma
Dec 2015**

**PD-1
Monotherapy
Reimbursed**

**PD-1
Monotherapy
Access**

**PD-1 + CTLA-4
Combination**



Nivolumab + Ipilimumab in Melanoma:PFS (Intent-to-Treat)



	NIVO + IPI (N=314)	NIVO (N=316)	IPI (N=315)
Median PFS, months (95% CI)	11.5 (8.9–16.7)	6.9 (4.3–9.5)	2.9 (2.8–3.4)

However!

- No overall survival data available in the public domain at this point.
- 55% rate of Grade 3-4 treatment-related adverse events
- Study was designed to compare nivo+ipi to ipi but clinically nivo+ipi versus nivo is the relevant comparison.

No. at Risk		months						
NIVO + IPI	314	219	173	151	65	11	1	0
NIVO	316	177	147	124	50	9	1	0
IPI	315	137	77	54	24	4	0	0



Cost-Effectiveness of Nivolumab in combination with Ipilimumab in patients with unresectable advanced melanoma in Australia

M Bohensky, H Kim, A Gorelik, D Liew

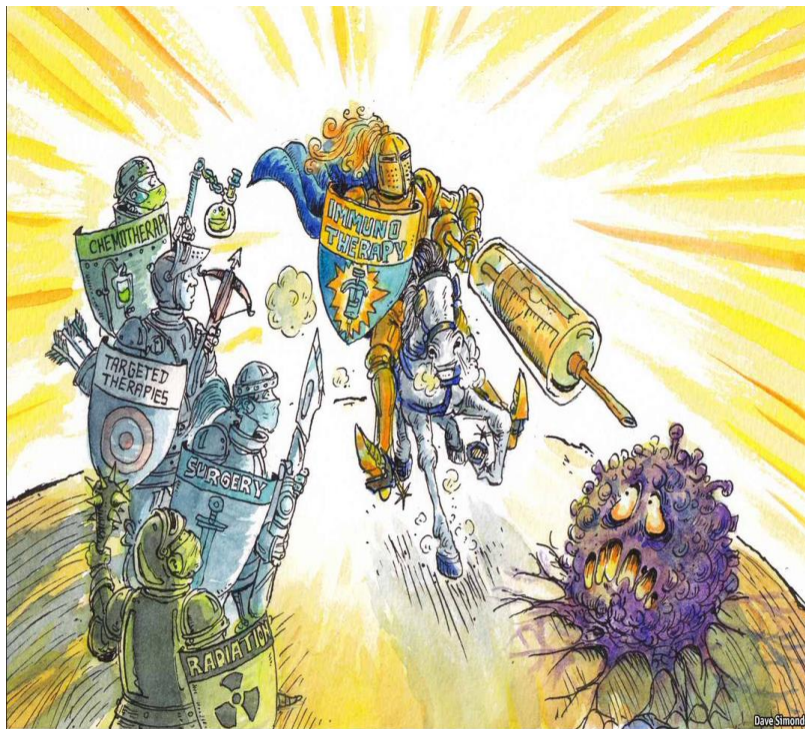
The University of Melbourne
Bristol Myers Squibb Australia

Key findings

- Comparing Nivo+Ipi to Ipi
 - \$US38,000 per life year gained
 - \$US45,000 per QALY gained
- Within ICER acceptable to NICE/PBAC
(UK \$US45,000 / Aus \$US 54,000)

Limitations

- Clinically, and health economically, the most relevant comparison is nivo + ipi v nivo
- Only a model - no overall survival data at this point
- Model used the relationship between PFS and OS based predominantly on BRAF & MEK inhibitors. IO agents maybe different.
- Details of costings of toxicity not provided to give a clinician confidence of the accuracy



Oncology

And then there were five

CHICAGO

Doctors are trying—with some success—to recruit the immune system to help with the war on cancer

The Economist

JUNE 6TH–12TH 2015

Economist.com

A fifth way to fight cancer

How to power Africa

Shinzo Abe, shareholder activist

Time to privatise India's banks

Beyond Blatter

**We need a 6th way
to fight cancer:
Innovative health
economics!**

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