SITC 2016

NATIONAL HARBOR, MD
NOVEMBER 9–13, 2016

Cobimetinib in Combination with Atezolizumab

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Society for Immunotherapy of Cancer

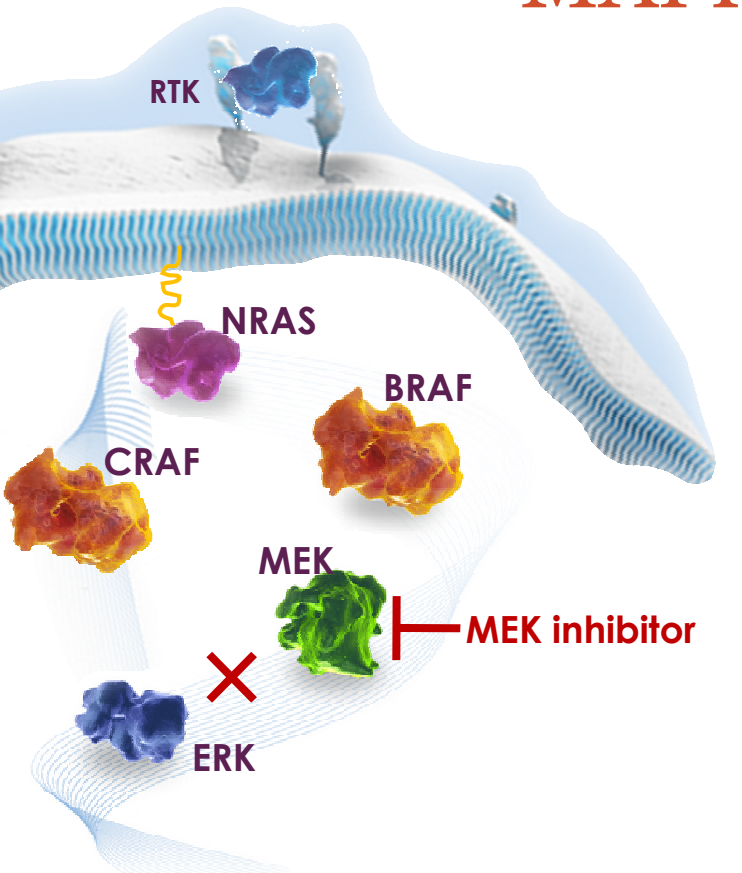
Presenter Disclosure Information

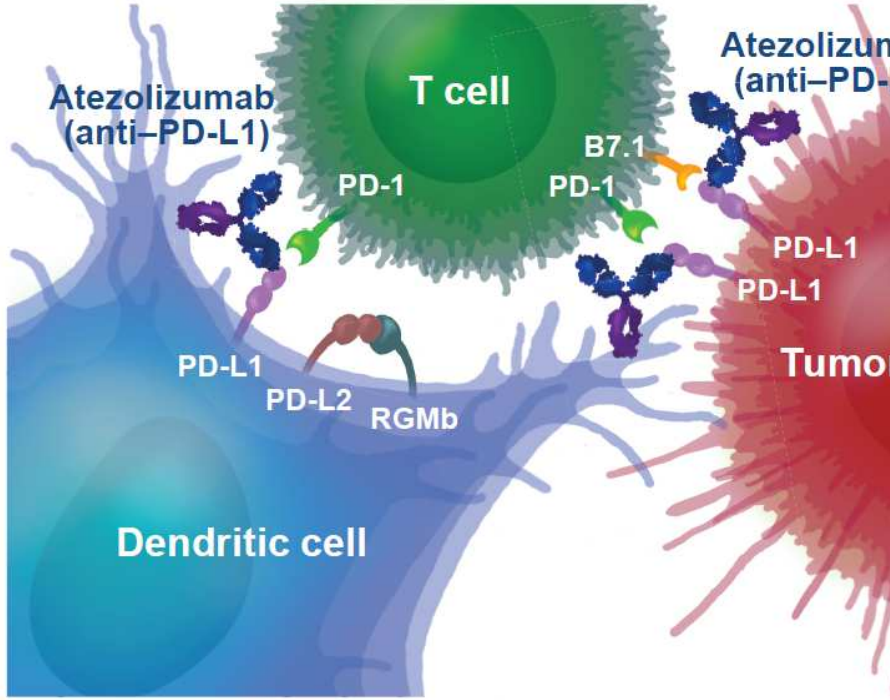
Edward Cha, MD, PhD

The following relationships exist related to this presentation:

Genentech – Roche: Employee, Salary, Stock

MAPK and PD-L1 Inhibition



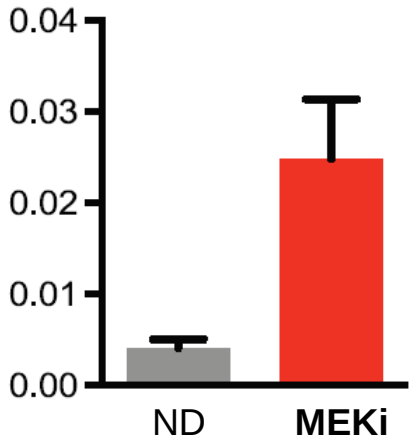


imetinib is a reversible, potent and selective inhibitor of
K1 and MEK2

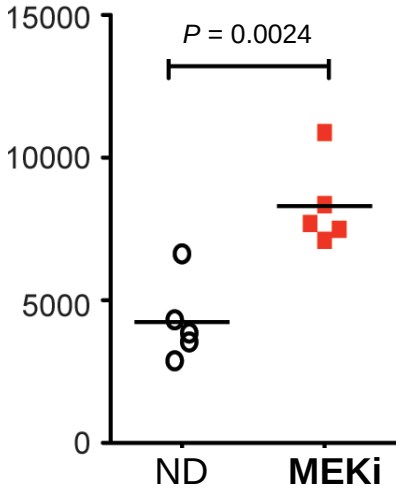
- **Atezolizumab** prevents binding of PD-L1 to its
PD-1 and B7.1 (CD80), **thereby restoring tum**
specific T-cell immunity

Blocking MEK Signaling Results in Changes in the Tumor Microenvironment

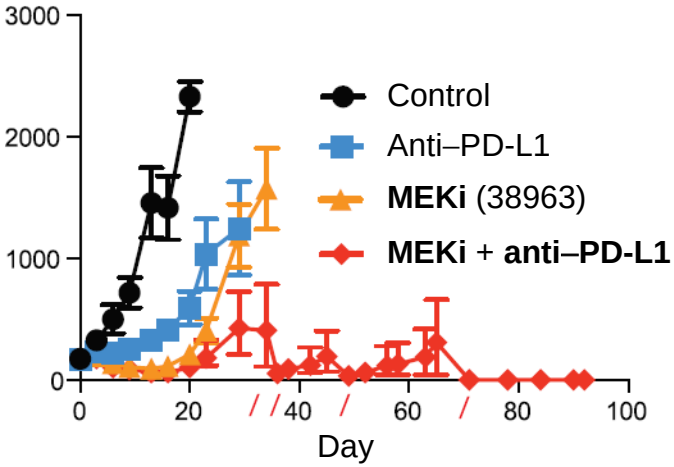
CD8+ T cell per Tumor Cell



Class I MHC



Tumor Volume (mm^3)



ntratumoral T cell accumulation

⬇ TCR-induced T-cell death

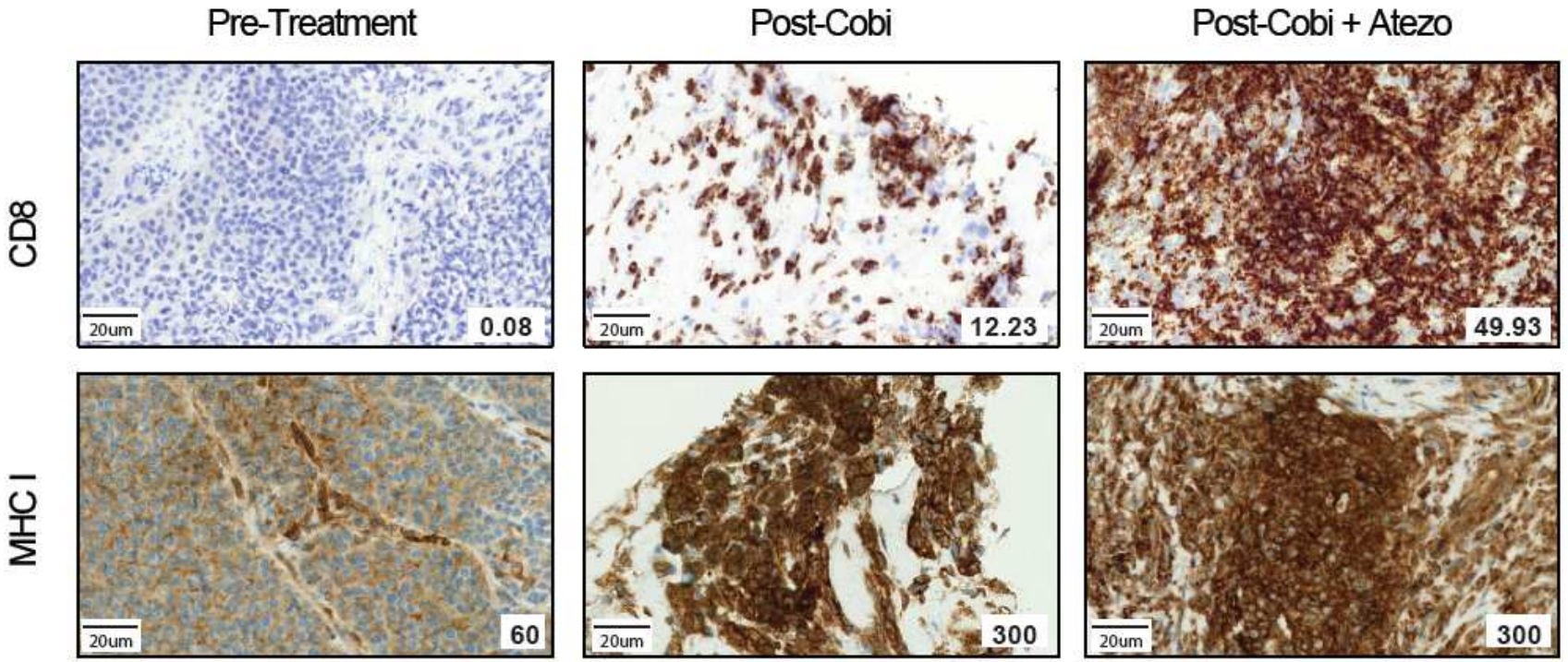
MHC I upregulation

Efficacy with anti-PDL1
(CT26 syngeneic mouse model)

MEKi, MEK inhibitor; ND, no drug (vehicle alone); TCR, T-cell receptor.

Ebert P et al. I

D8+ T-cells and MHC I Expression with MEK and PD-L1 Inhibiti



- Atezolizumab + cobimetinib combination increased intratumoral CD8+ T-cell accumulation and MHC I expression in patient with clear cell sarcoma, who achieved a PR

The numbers in the CD8 panel denote percentages of CD8+ cells. The numbers in the MHCI panel indicate the H-score.

Bendell J et a
Desai J et a

Safety Summary of Cobimetinib + Atezolizumab

Patients with mCRC (n=23)

Parameter	Treatment-related, n (%)
All grade	23 (100)
Grade 3 AEs	8 (35)
Grade 4 AEs	1 (4)
Grade 5 AEs	0 (–)
Serious AEs	2 (9)
AEs leading to withdrawal from cobimetinib	4 (17)
AEs leading to withdrawal from atezolizumab	0 (–)

bimetinib + atezolizumab had a manageable safety profile similar to that observed with either agent

all-cause or treatment-related Grade 5 events were observed

One treatment-related Grade 4 blood increase in creatine phosphokinase was observed

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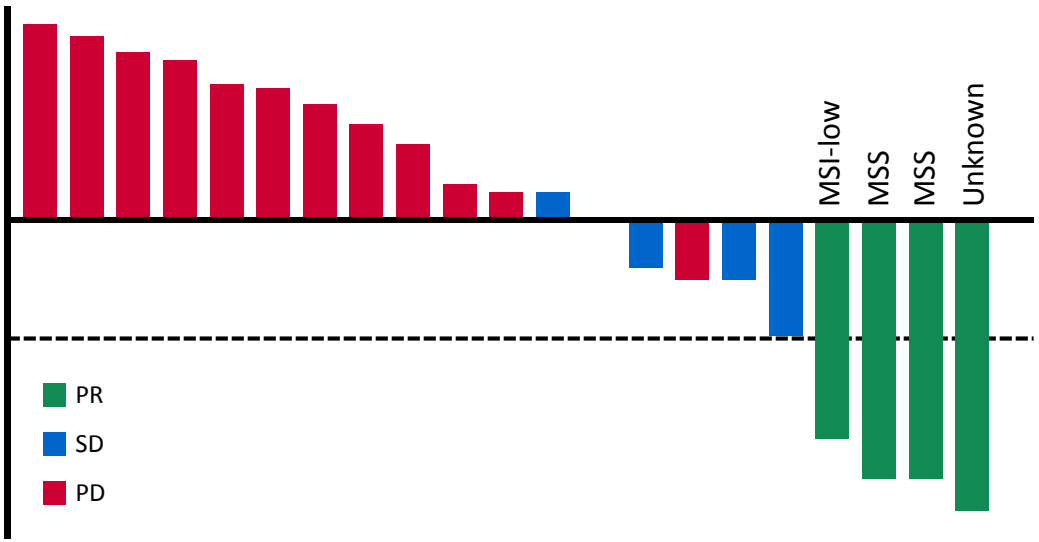
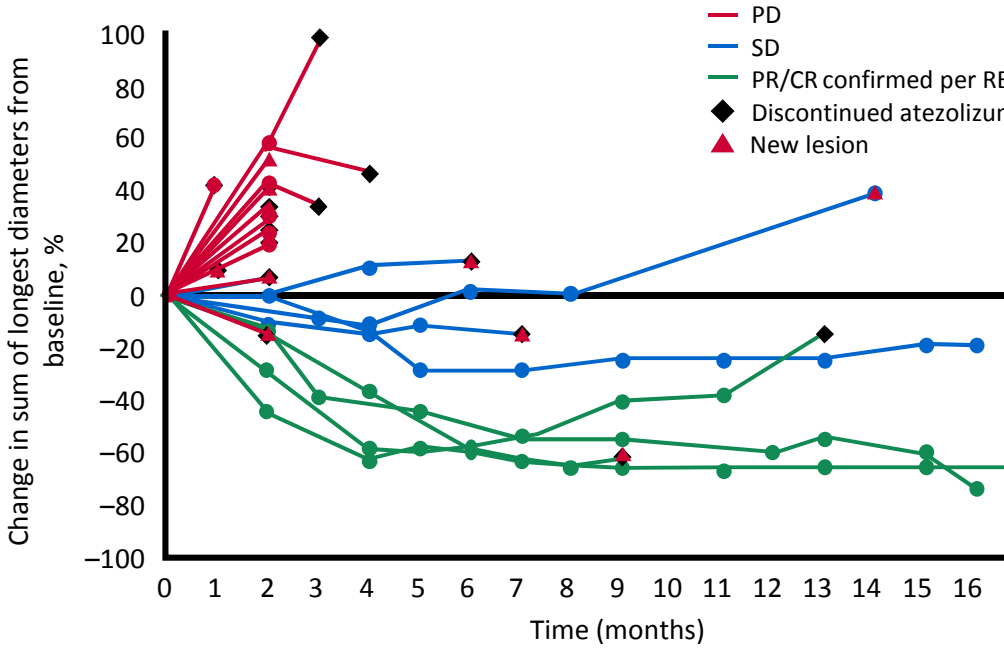
Cobimetinib and Atezolizumab Efficacy: Colorectal (CRC)





Efficacy endpoints	N = 23
ORR, % (95% CI)	17% (5%, 39%)
PFS, median (95% CI)	2.3 mo (1.8, 9.5)
1-year OS, % (95% CI)	61% (39%, 84%)

- Four patients had partial responses (confirmed per RECIST responses are ongoing in two of these patients
- Median duration of response was not reached (range: 5.4–1 months)

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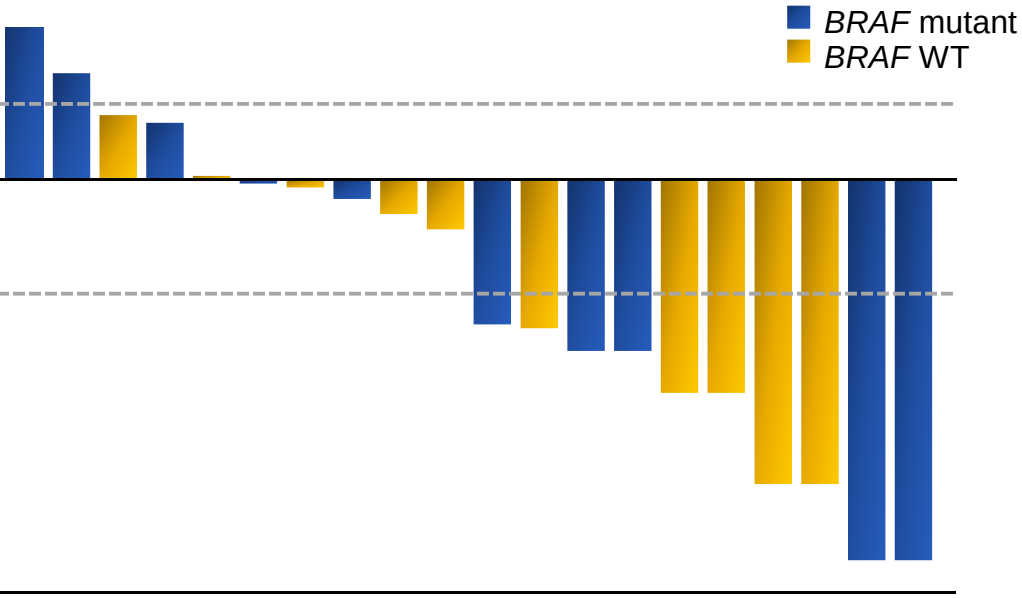
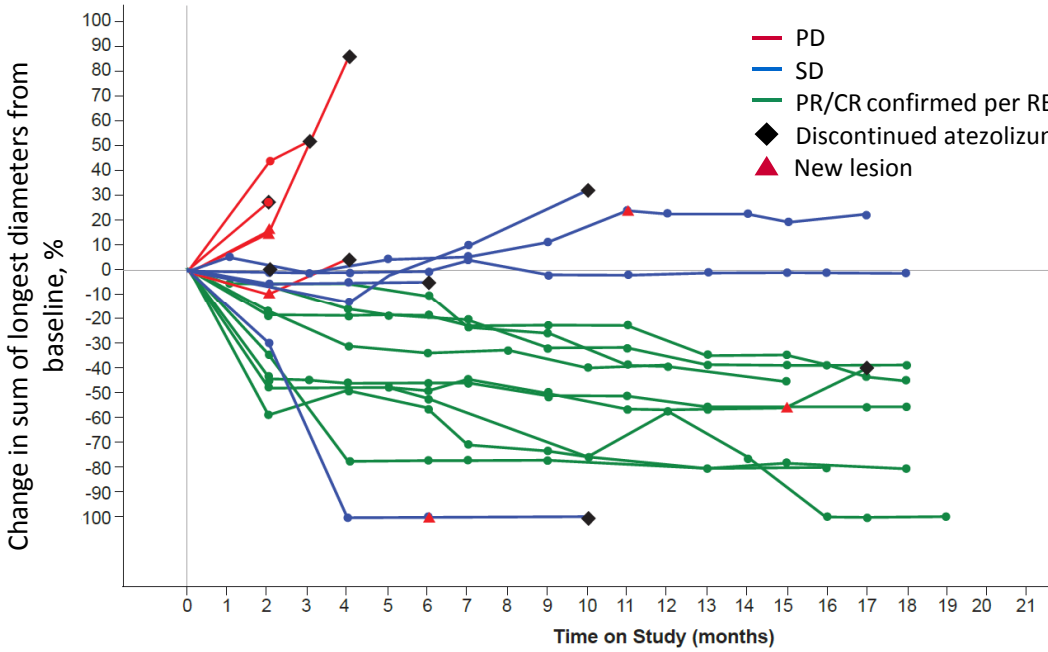
Desai J et al

Cobimetinib and Atezolizumab Efficacy: Melanoma





Efficacy endpoints	N = 20
ORR, % (95% CI)	45% (23%, 69%)
PFS, median (95% CI)	12.0 mo (2.8, NE)
1-year OS, % (95% CI)	85% (69%, 100%)

- Nine patients had partial responses (confirmed per RECIST median duration of response is 14.9 mo
- mPFS was 11.9 mo in *BRAF* mutant patients and 15.7 mo i patients

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Summary

Selective inhibition of MEK signaling can sensitize tumors to anti-PDL1 by promoting intratumoral CD8+ T-cell accumulation and MHC I expression

Cobimetinib + atezolizumab had a manageable safety profile similar to that observed with either agent

Cobimetinib + atezolizumab demonstrated encouraging antitumor activity

In mCRC, responses were observed in patients with microsatellite-stable tumors

In melanoma, clinical benefit of cobimetinib + atezolizumab was seen regardless of *BRAF* status

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