New therapies for melanoma: understanding cancer biology translates into new therapies

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Unraveling the cancer genome
BRAF mutations in human cancer

June, 2002: BRAF mutations in 7% of cancer

PET Scans at Baseline and Day 15 on vemurafenib
Maximal tumor shrinkage by individual patient

Vemurafenib
Maximal tumor shrinkage by individual patient

Percent change from baseline in sum of tumor diameters

Dacarbazine
Overall survival (1st interim analysis)

Vemurafenib (N=336)
Est 6 mo survival 84%

Dacarbazine (N=336)
Est 6 mo survival 64%

Hazard ratio 0.37
(95% CI; 0.26 - 0.55)
Log-rank P<0.0001

No. of patients in follow up
Dacarbazine 336 283 192 137 98 64 39 20 9 1 1
Vemurafenib 336 320 266 210 162 111 80 35 14 6 1
Understanding the consequences of cancer molecular biology
Immunologic interface: the breaks

Dendritic cell

MHC

B7-1 (CD80)

B7-2 (CD86)

PD-L1 (B7-H1)

T cell

CD28

receptor

PD-1

CTLA4

- +
Pre-treatment

Week 12 (10/06)

4 doses ipilimumab

No drug

12/06

5/07

12/06

5/07

Courtesy J. Wolchok (MSK)
Ipilimumab phase III trial

Investment in cancer research is paying off for patients now