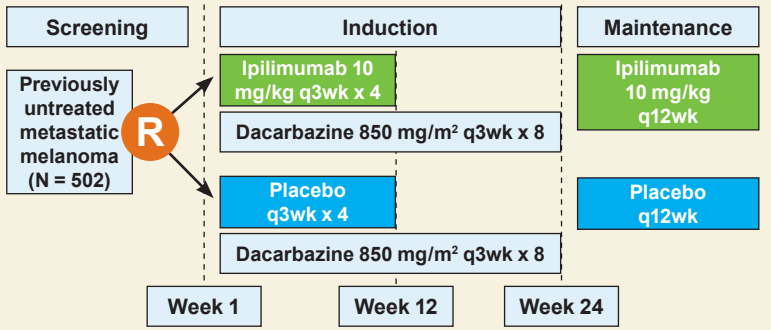
Phase 3 Randomized Study of Ipilimumab (IPI) plus Dacarbazine (DTIC) vs DTIC Alone as First-Line Treatment in Patients with Unresectable Stage III or IV Melanoma

Wolchok J et al.

Proc ASCO 2011;Abstract LBA5.

Study 024: A Phase III Placebo-Controlled Trial of First-Line DTIC ± IPI (10 mg/kg)



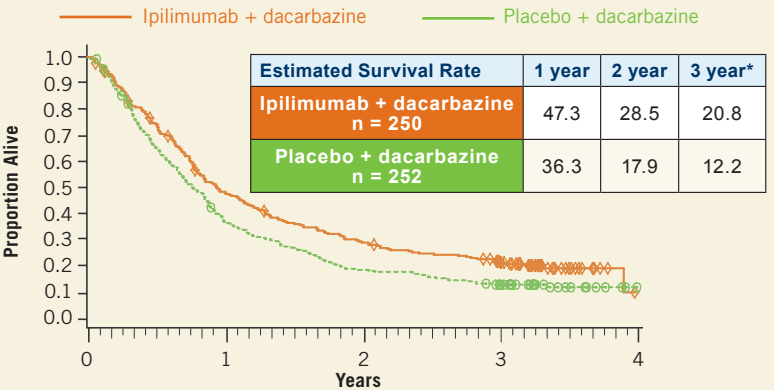
Wolchok J et al. *Proc ASCO* 2011;Abstract LBA5.

Study 024: Response and Survival

Clinical parameter	DTIC + placebo (n = 252)	IPI + DTIC (n = 250)	Hazard ratio	*p*-value
Median overall survival	9.1 mo	11.2 mo	0.72	0.0009
Disease control rate	30.2%	33.2%	—	—
Best overall response Complete response Partial response Stable disease	10.3% 0.8% 9.5% 19.8%	15.2% 1.6% 13.6% 18.0%	—	—
Duration of response	**8.1 mo**	**19.3 mo**	**—**	**—**

Wolchok J et al. *Proc ASCO* 2011;Abstract LBA5.

Study 024: Overall Survival



Estimated Survival Rate	1 year	2 year	3 year*
Ipilimumab + dacarbazine n = 250	47.3	28.5	20.8
Placebo + dacarbazine n = 252	36.3	17.9	12.2

* 3-year survival was a post-hoc analysis

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Study 024: Safety Summary

- **Types of adverse events associated with IPI consistent with previous studies**
  - **— Mainly affect skin, GI tract, liver, endocrine system**
- **Mechanism (immune)-based:**
  - **— Managed with established guidelines**
  - **— Generally responsive to dose interruptions/discontinuation, corticosteroids and/or other immunosuppressants**
- **Rates of high-grade events with IPI + DTIC were different from those observed in Phase II**
  - **— Elevated AST (21.9%) and ALT (18.2%) — higher (Phase II data not available)**
  - **— Diarrhea (4.0% vs 25.7%) and colitis (2.0% vs 2.9%)**
  - **— No GI perforations**

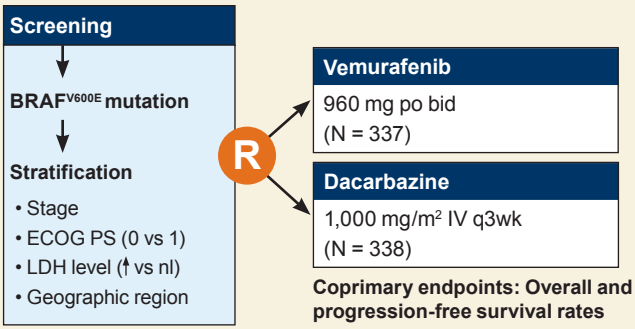
Wolchok J et al. *Proc ASCO* 2011;Abstract LBA5.

Improved Survival with Vemurafenib in Melanoma with BRAF V600E Mutation

Chapman PB et al.

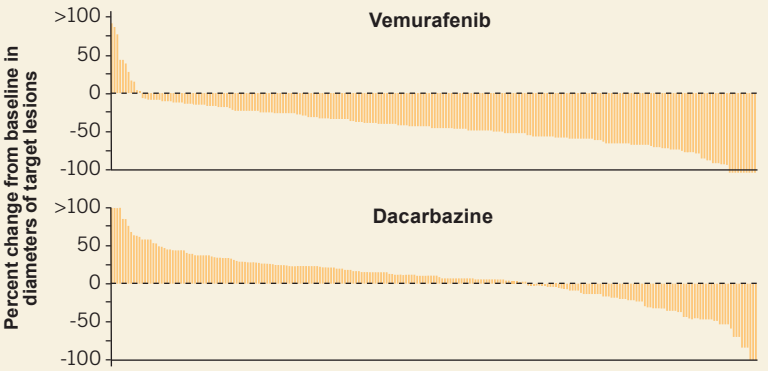
N Engl J Med 2011;364(26):2507-16.

BRIM3: A Phase III Trial of BRAF Inhibitor Vemurafenib versus DTIC in BRAF^{V600E}-Mutated Melanoma



Chapman PB et al. *N Engl J Med* 2011;364(26):2507-16.

Maximal Tumor Shrinkage by Individual Patient



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BRIM3: Efficacy Results

Clinical parameter	DTIC	Vemurafenib	HR	*p*-value
ORR (n = 220, 219) CR PR	5.0% 0% 5.0%	48.0% 0.9% 47.5%	—	<0.001
Estimated six-month OS rate (n = 336, 336)	64%	84%	0.37	<0.001
Median PFS (n = 274, 275)	1.6 mo	5.3 mo	0.26	<0.001

HR = hazard ratio; ORR = overall response rate; CR = complete response; PR = partial response; OS = overall survival; PFS = progression-free survival

Chapman PB et al. *N Engl J Med* 2011;364(26):2507-16.

BRIM3: Select Adverse Events

Adverse event, %	DTIC (n = 282)		Vemurafenib (n = 336)	
	Grade 2	Grade 3	Grade 2	Grade 3
Arthralgia	<1%	<1%	18%	3%
Rash	0%	0%	10%	8%
Cutaneous squamous cell carcinoma	—	<1%	—	12%
Keratoacanthoma	0%	0%	2%	6%

- ≥Grade 4 adverse events in vemurafenib arm: Neutropenia (<1%)

Chapman PB et al. *N Engl J Med* 2011;364(26):2507-16.