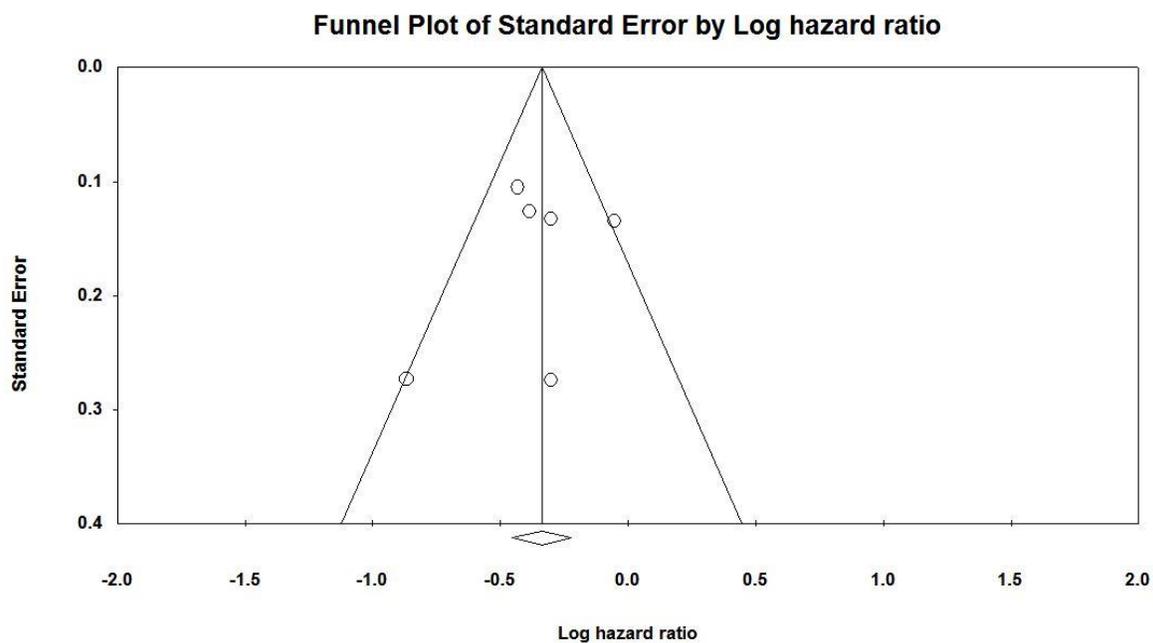
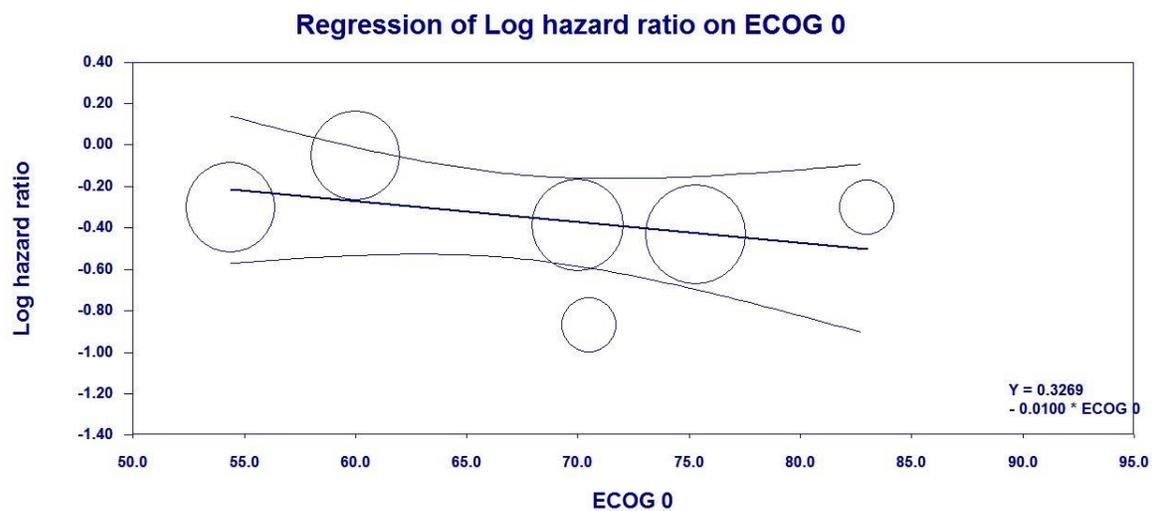


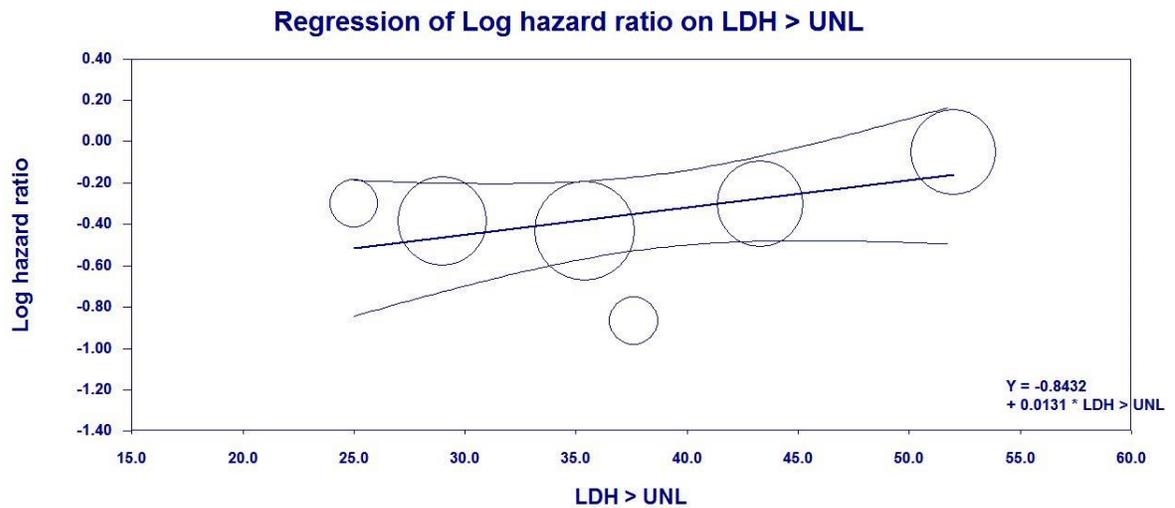
Supplementary Figure 1. Funnel plot.



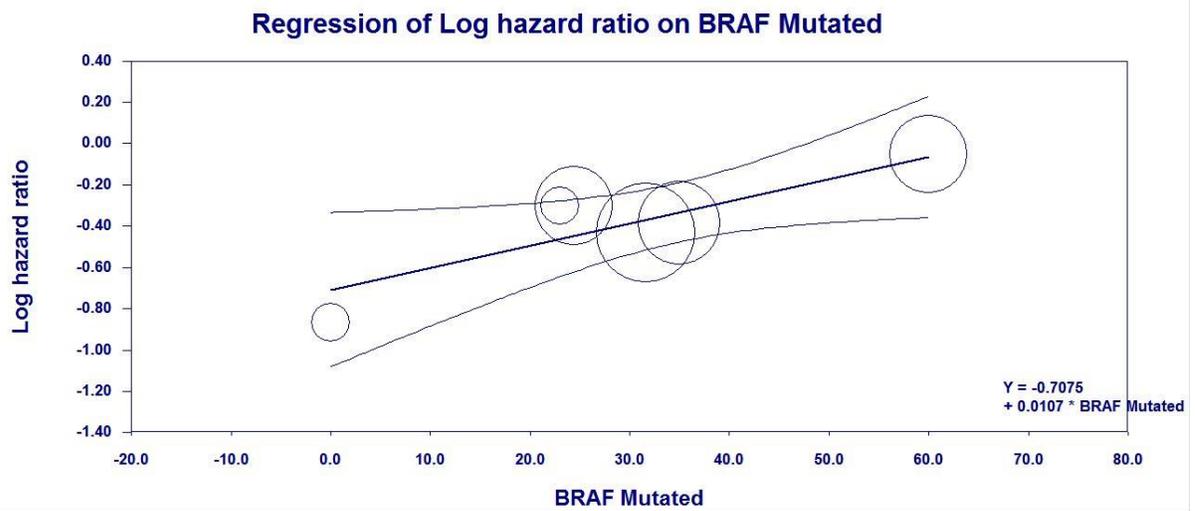
Supplementary Figure 2. Scatter plot of meta-regression using ECOG status.



Supplementary Figure 3. Scatter plot of meta-regression using LDH status.



Supplementary Figure 4. Scatter plot of meta-regression using BRAF mutated status.



Supplementary Table1. Search Strategy for meta-analysis.

Database	Search Strategy	Number of citations
Cochrane Library	ALL (metastatic AND melanoma OR advance AND melanoma) AND ALL(anti-programmed AND cell AND death AND receptor AND 1 AND monoclonal AND antibody OR anti-PD-1 AND monoclonal AND antibody OR PD-1 OR pembrolizumab OR nivolumab)	128
Scopus	ALL (metastatic melanoma OR advance melanoma) AND ALL(anti-programmed cell death receptor 1 monoclonal antibody OR anti-PD-1 monoclonal antibody OR PD-1 OR pembrolizumab OR nivolumab)	1497
PubMed	#1: all field (metastatic melanoma) OR all field (advance melanoma). #2: all field (anti-programmed cell death receptor 1 monoclonal antibody) OR all field (anti-PD-1 monoclonal antibody) OR all field (PD-1) OR all field (pembrolizumab) OR all field (nivolumab) #3: #1 AND #2	853
Clinicaltrial.gov	Condition or disease: metastatic melanoma OR advance Melanoma Other terms: anti-programmed cell death receptor 1 monoclonal antibody OR anti-PD-1 monoclonal antibody OR PD-1 OR pembrolizumab OR nivolumab Study type: All studies.	150

Supplementary Table 2. List of studies with high risk of Bias.

Study Identification	Reason for possible high risk of bias.
KEYNOTE 002 NCT0170428	Inherent bias associated with phase II studies including selection and publication bias.
KEYNOTE 006 NCT01866319	Neither the treating physician nor the patients were blinded leading to high risk for bias.
CheckMate 066 NCT01721772	Study only included patients with wild BRAF and treatment naïve patients.

List of Abbreviations.

ABBREVIATION	EXPANSION
BRAF gene	B- Rapidly Accelerated Fibrosarcoma gene
CTLA-4	Cytotoxic T lymphocyte antigen-4
CM	CheckMate
ECOG	Eastern Cooperative Oncology Group
US FDA	United states Food and drug administration
HR	Hazard ratio
KN	KEYNOTE
LDH	Lactate dehydrogenase
MEK	Mitogen-activated kinase
NCCN	National Comprehensive Cancer Network
OS	Overall Survival
PD1	Programed cell death 1
PDL	Programed cell death ligand
PFS	Progression Free Survival
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PICOS	Population. Intervention. Comparison. Outcome. Study Design
SEER	Surveillance, Epidemiology, and End Results
ULN	Upper level of normal.