Figure 1

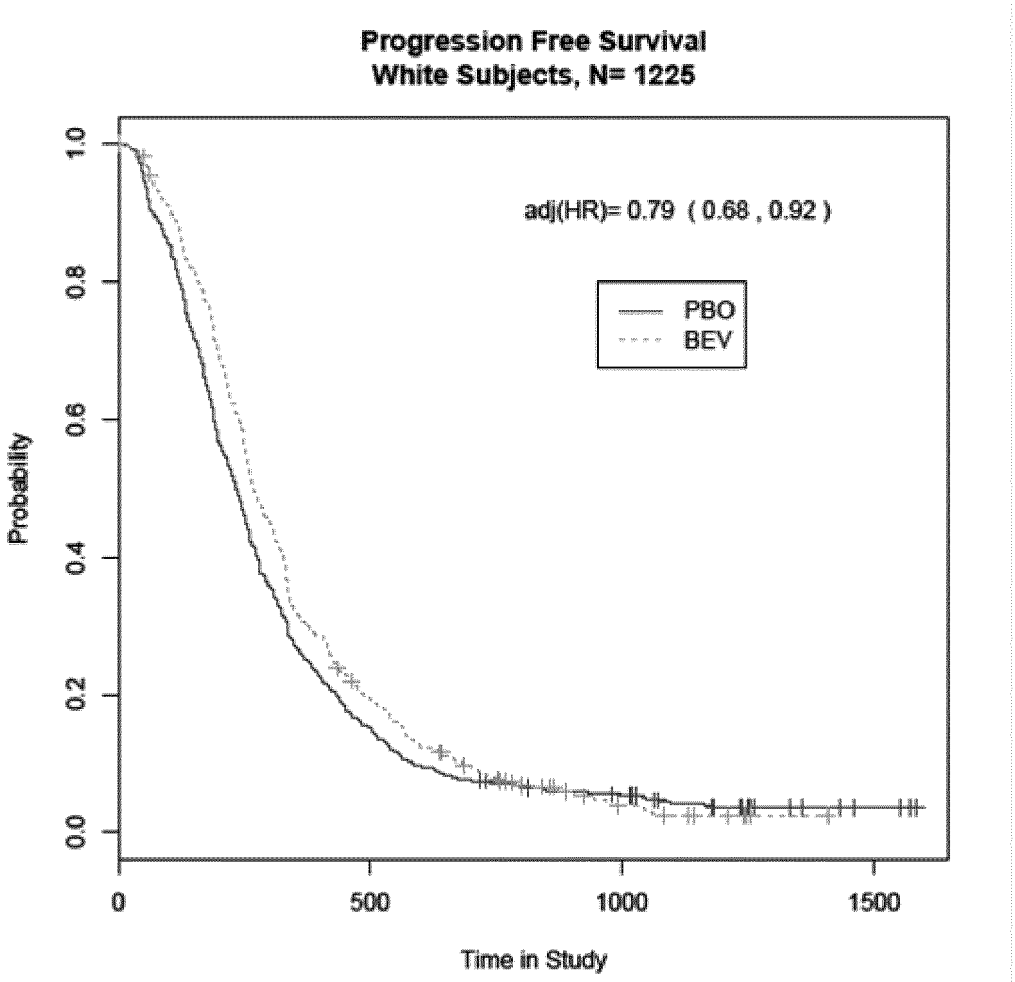

Progression Free Survival
White Subjects, N= 1225
adj(HR)= 0.79 (0.68 , 0.92)
PBO
BEV
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
500
1000
1500
Time in Study

Figure 2

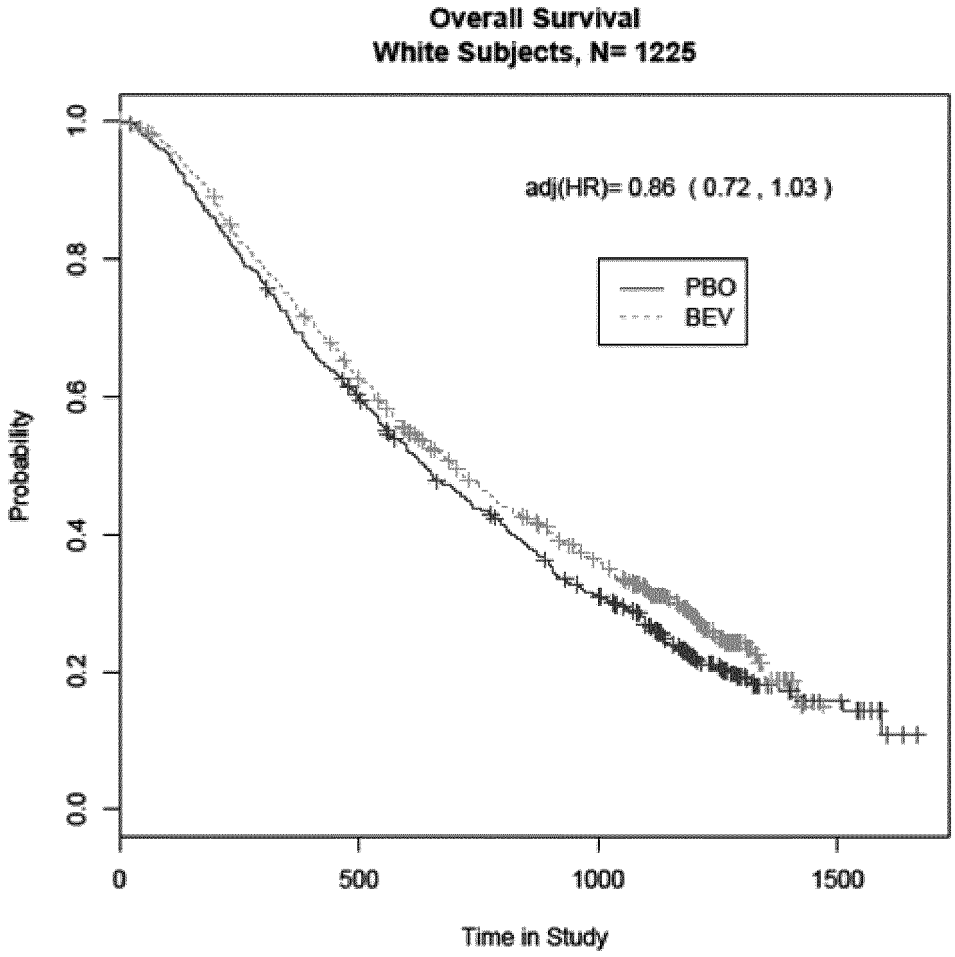

Overall Survival
White Subjects, N= 1225
adj(HR)= 0.86 (0.72 , 1.03)
PBO
BEV
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
500
1000
1500
Time in Study

Figure 3

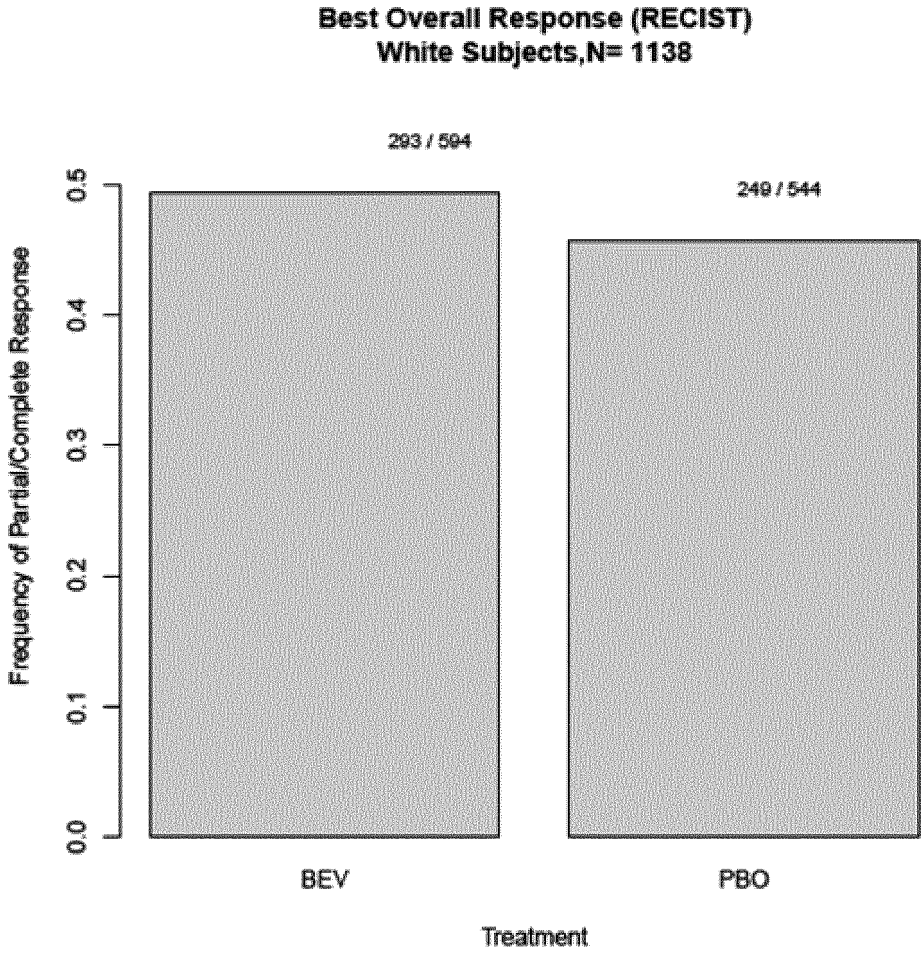

Best Overall Response (RECIST)
White Subjects,N= 1138
293 / 594
249 / 544
Frequency of Partial/Complete Response
0.0
0.1
0.2
0.3
0.4
0.5
BEV
PBO
Treatment

Figure 4

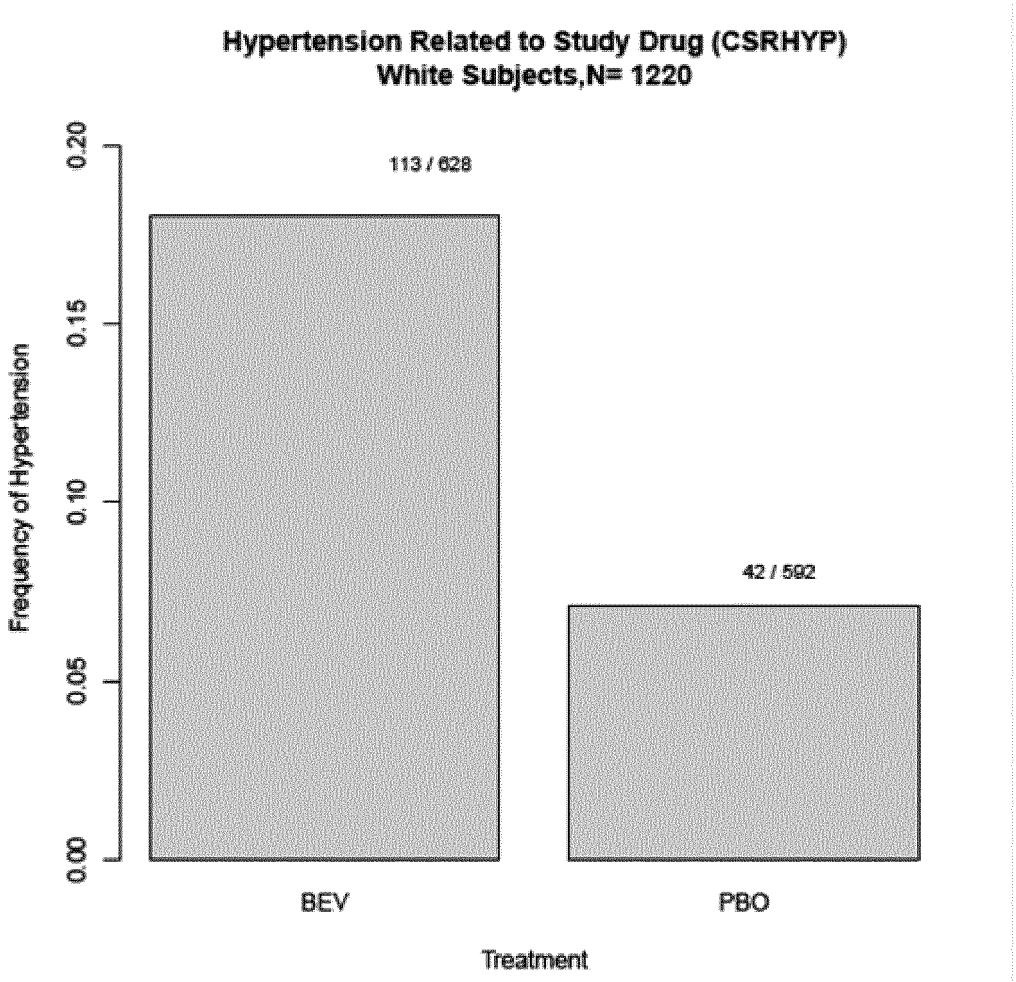

Hypertension Related to Study Drug (CSRHYP)
White Subjects,N= 1220
113 / 628
42 / 592
Frequency of Hypertension
0.00
0.05
0.10
0.15
0.20
BEV
PBO
Treatment

Figure 5

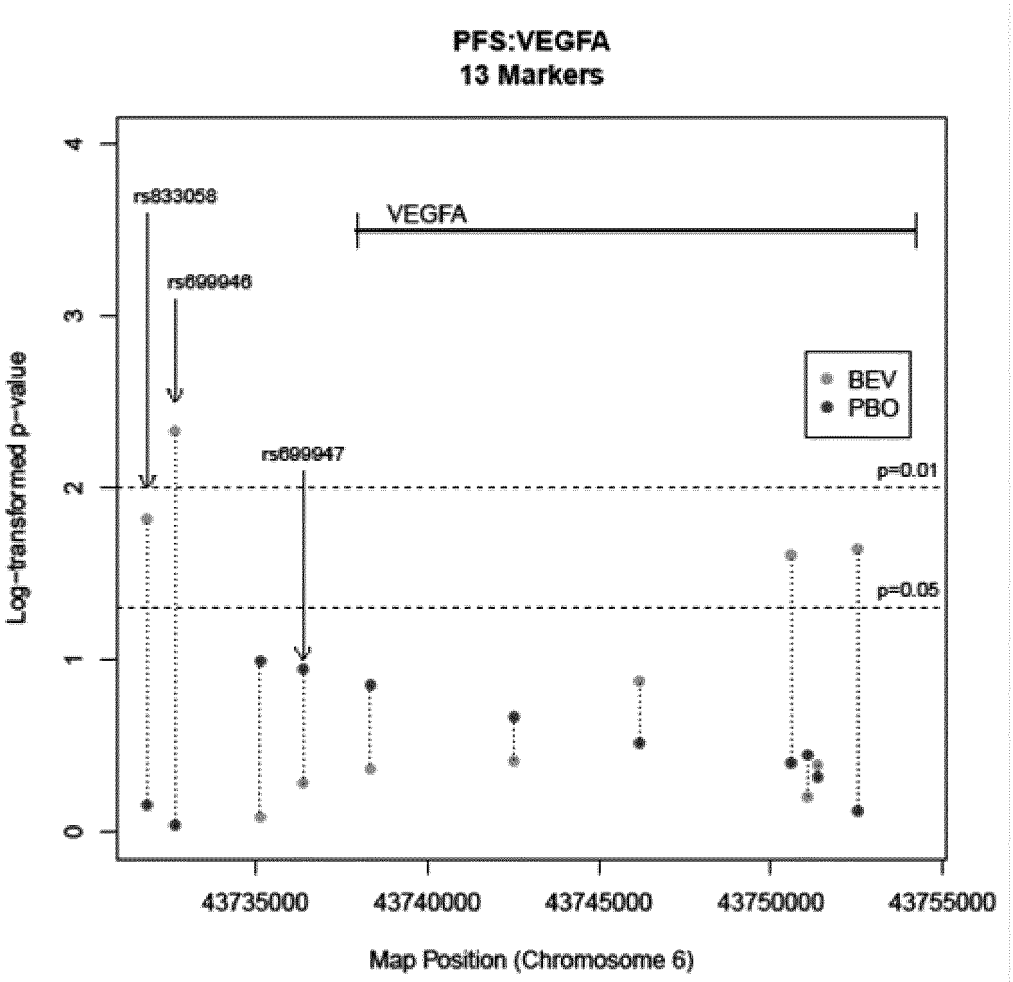

PFS:VEGFA
13 Markers
VEGFA
rs833058
rs699946
rs699947
BEV
PBO
p=0.01
p=0.05
Log-transformed p-value
0
1
2
3
4
43735000
43740000
43745000
43750000
43755000
Map Position (Chromosome 6)

Figure 6

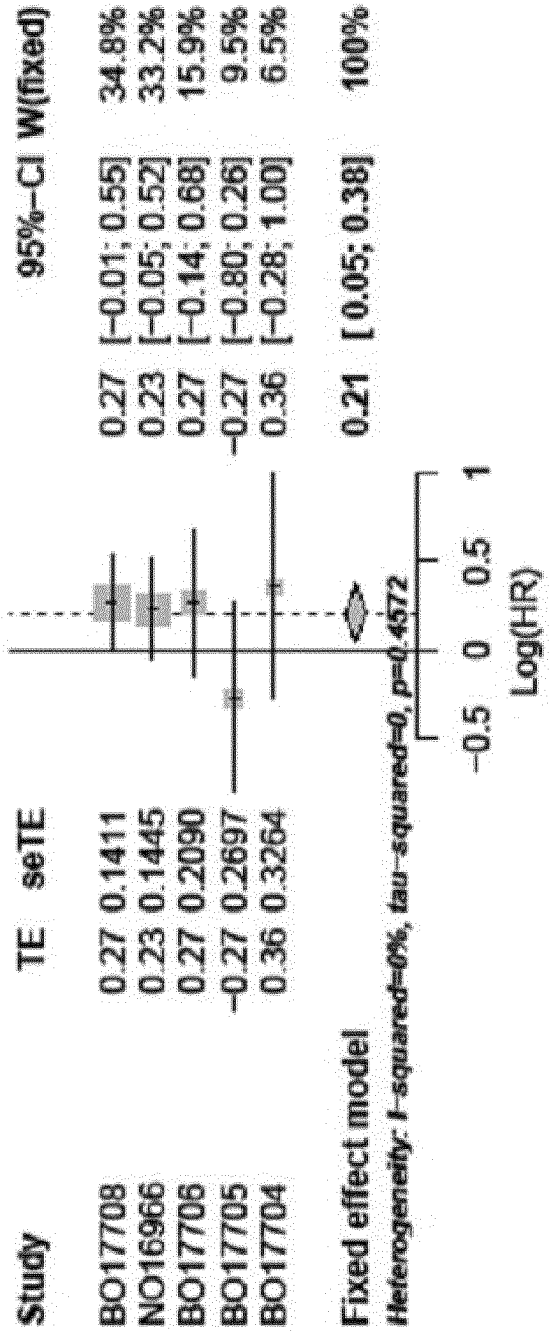

Study
TE seTE
95%−CI W(fixed)
BO17708 0.27 0.1411 0.27 [−0.01; 0.55] 34.8%
NO16966 0.23 0.1445 0.23 [−0.05; 0.52] 33.2%
BO17706 0.27 0.2090 0.27 [−0.14; 0.68] 15.9%
BO17705 −0.27 0.2697 −0.27 [−0.80; 0.26] 9.5%
BO17704 0.36 0.3264 0.36 [−0.28; 1.00] 6.5%
Fixed effect model 0.21 [0.05; 0.38] 100%
Heterogeneity: I−squared=0%, tau−squared=0, p=0.4572
−0.5 0 0.5 1
Log(HR)

Figure 7

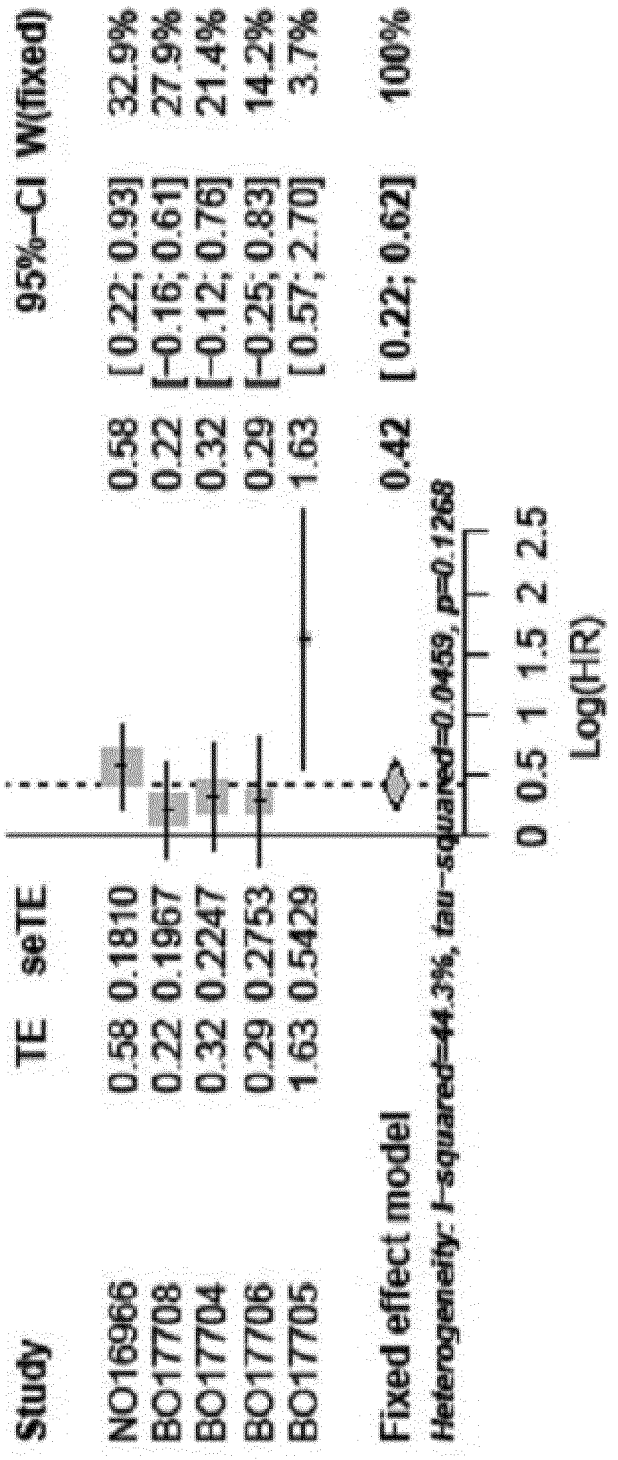

Study
TE
seTE
95%–CI
W(fixed)
NO16966 0.58 0.1810 0.58 [0.22; 0.93] 32.9%
BO17708 0.22 0.1967 0.22 [–0.16; 0.61] 27.9%
BO17704 0.32 0.2247 0.32 [–0.12; 0.76] 21.4%
BO17706 0.29 0.2753 0.29 [–0.25; 0.83] 14.2%
BO17705 1.63 0.5429 1.63 [0.57; 2.70] 3.7%
Fixed effect model 0.42 [0.22; 0.62] 100%
Heterogeneity: I–squared=44.3%, tau–squared=0.0459, p=0.1263
0 0.5 1 1.5 2 2.5
Log(HR)

Figure 8

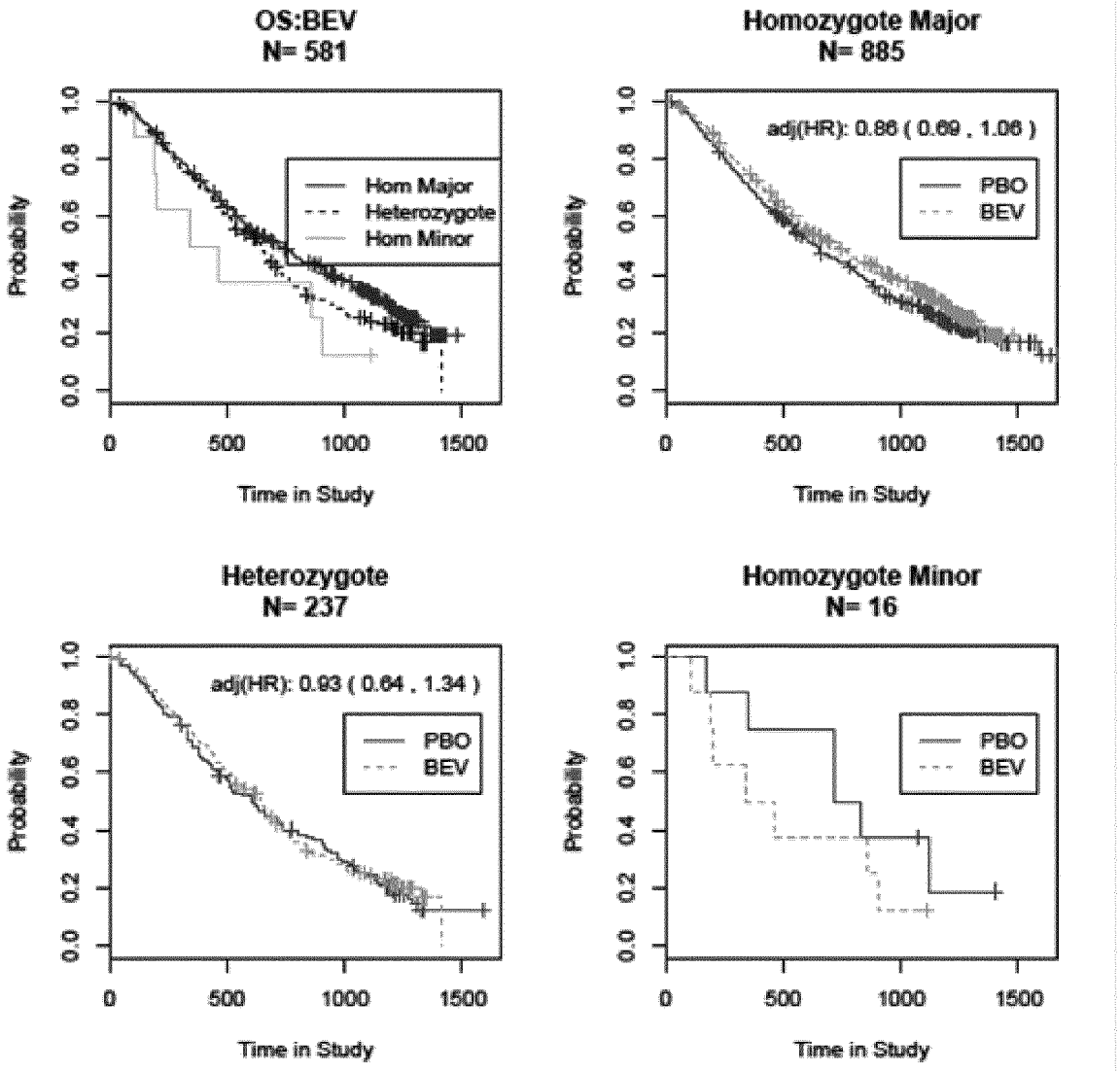

OS:BEV
N= 581
Hom Major
Heterozygote
Hom Minor
Probability
Time in Study
Homozygote Major
N= 885
adj(HR): 0.86 (0.69 , 1.06)
PBO
BEV
Heterozygote
N= 237
adj(HR): 0.93 (0.64 , 1.34)
Homozygote Minor
N= 16

Figure 9

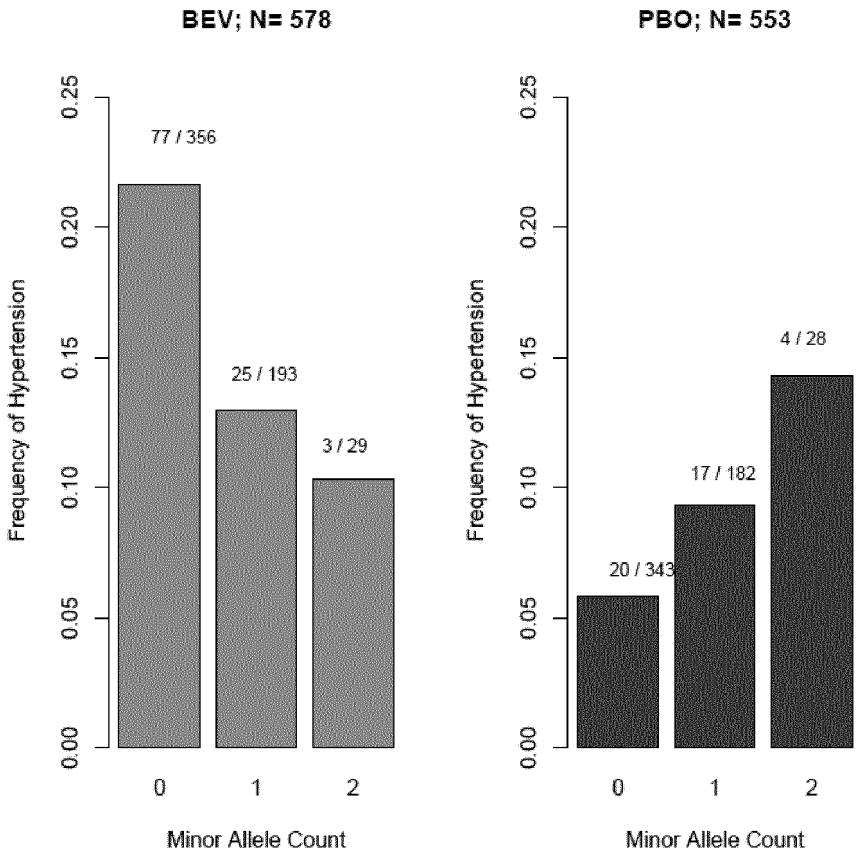

BEV; N= 578
Frequency of Hypertension
0.00
0.05
0.10
0.15
0.20
0.25
77 / 356
25 / 193
3 / 29
0
1
2
Minor Allele Count
PBO; N= 553
Frequency of Hypertension
0.00
0.05
0.10
0.15
0.20
0.25
20 / 343
17 / 182
4 / 28
0
1
2
Minor Allele Count

Figure 10

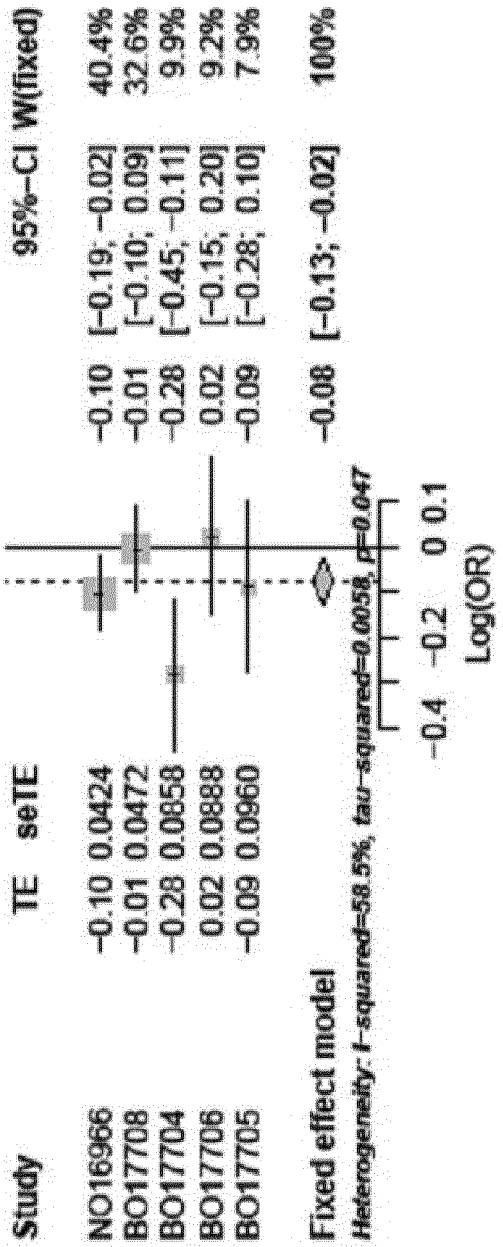

Study
TE seTE
95%−CI W(fixed)
NO16966 −0.10 0.0424 −0.10 [−0.19; −0.02] 40.4%
BO17708 −0.01 0.0472 −0.01 [−0.10; 0.09] 32.6%
BO17704 −0.28 0.0858 −0.28 [−0.45; −0.11] 9.9%
BO17706 0.02 0.0888 0.02 [−0.15; 0.20] 9.2%
BO17705 −0.09 0.0960 −0.09 [−0.28; 0.10] 7.9%
Fixed effect model −0.08 [−0.13; −0.02] 100%
Heterogeneity: I-squared=58.5%, tau-squared=0.0058, p=0.047
−0.4 −0.2 0 0.1
Log(OR)

Figure 11

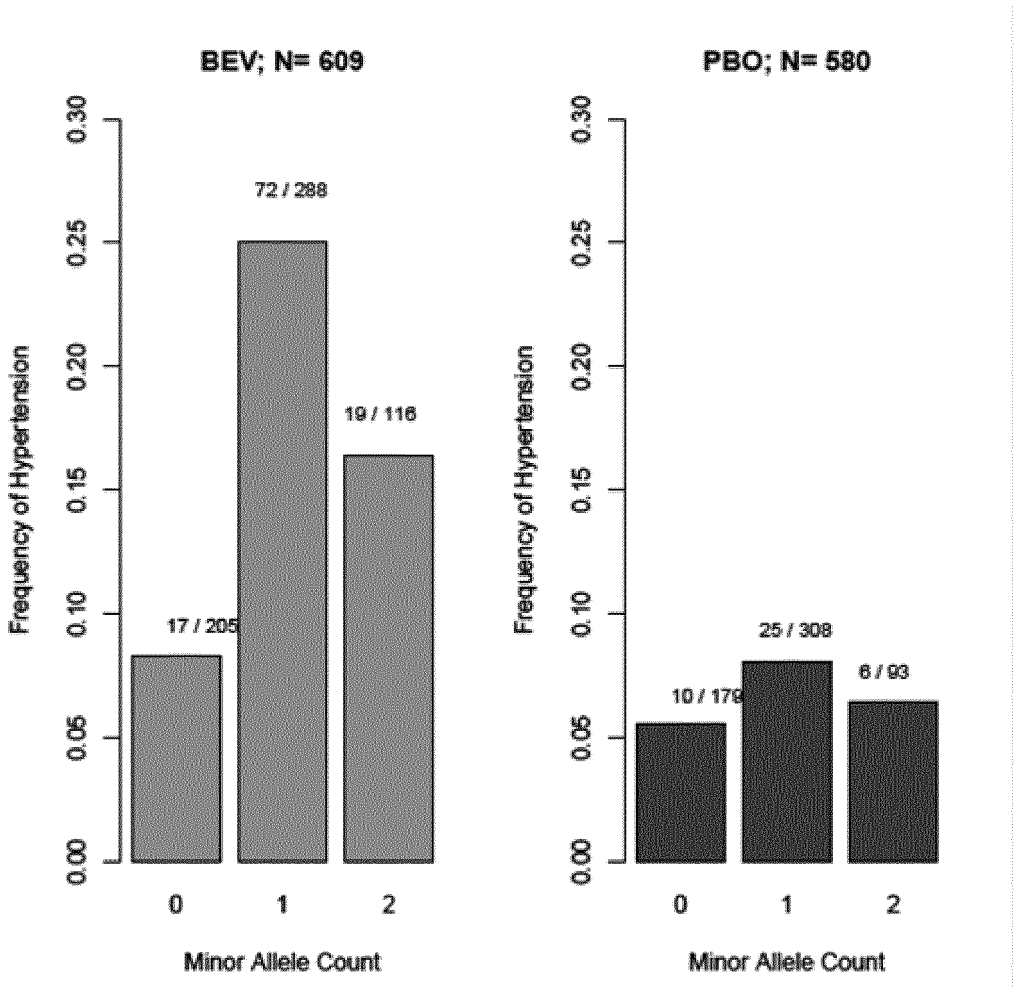

BEV; N= 609
Frequency of Hypertension
0.00
0.05
0.10
0.15
0.20
0.25
0.30
17 / 205
72 / 288
19 / 116
0
1
2
Minor Allele Count
PBO; N= 580
Frequency of Hypertension
0.00
0.05
0.10
0.15
0.20
0.25
0.30
10 / 179
25 / 308
6 / 93
0
1
2
Minor Allele Count

Figure 12

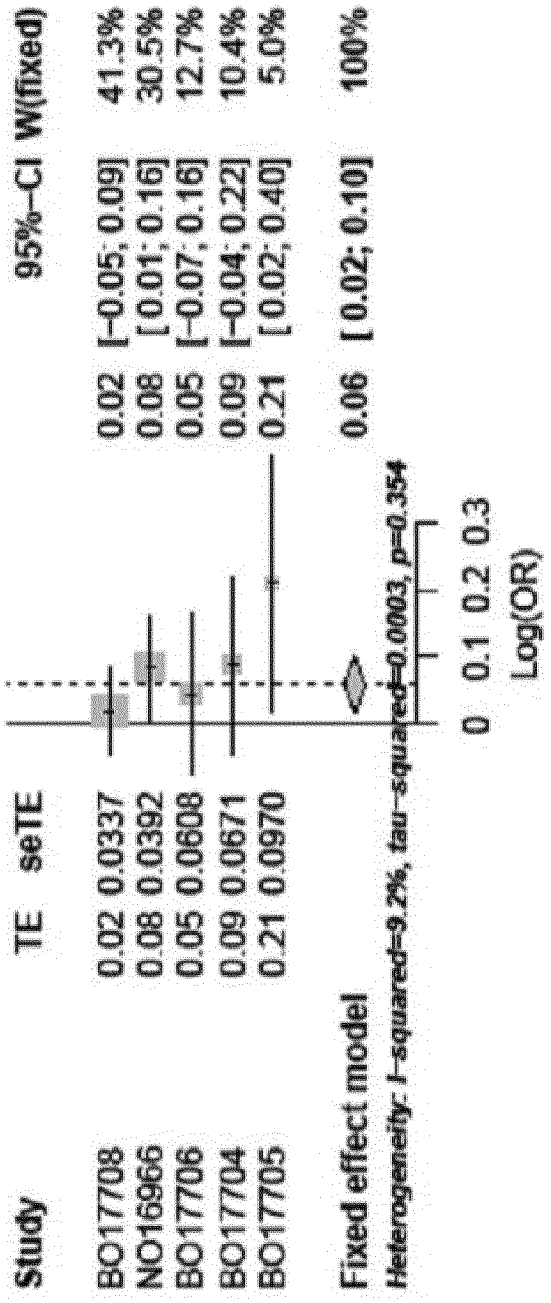

Study
TE seTE
95%–CI W(fixed)
BO17708 0.02 0.0337 0.02 [–0.05; 0.09] 41.3%
NO16966 0.08 0.0392 0.08 [0.01; 0.16] 30.5%
BO17706 0.05 0.0608 0.05 [–0.07; 0.16] 12.7%
BO17704 0.09 0.0671 0.09 [–0.04; 0.22] 10.4%
BO17705 0.21 0.0970 0.21 [0.02; 0.40] 5.0%
Fixed effect model 0.06 [0.02; 0.10] 100%
Heterogeneity: I–squared=9.2%, tau–squared=0.0003, p=0.354
0 0.1 0.2 0.3
Log(OR)

Figure 13

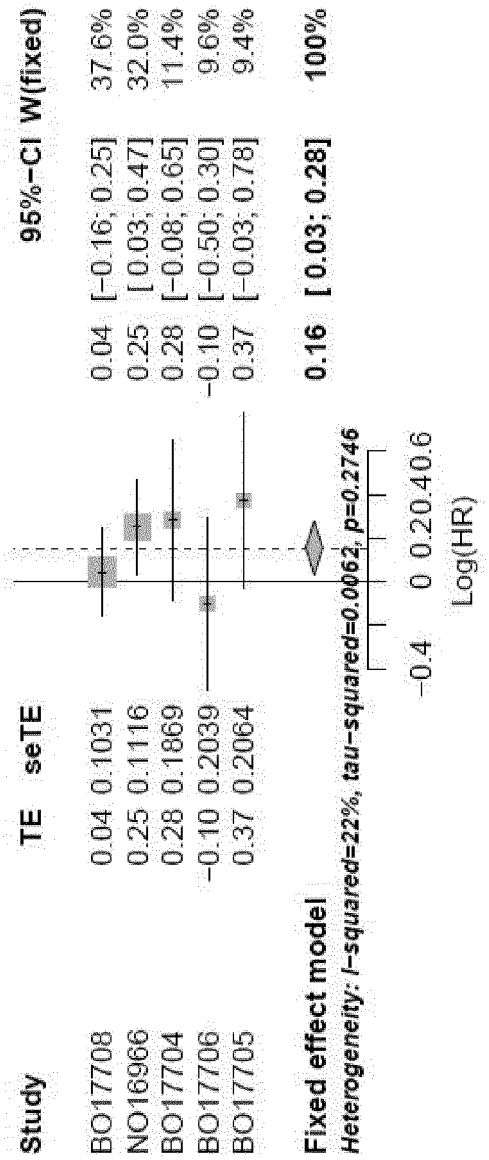
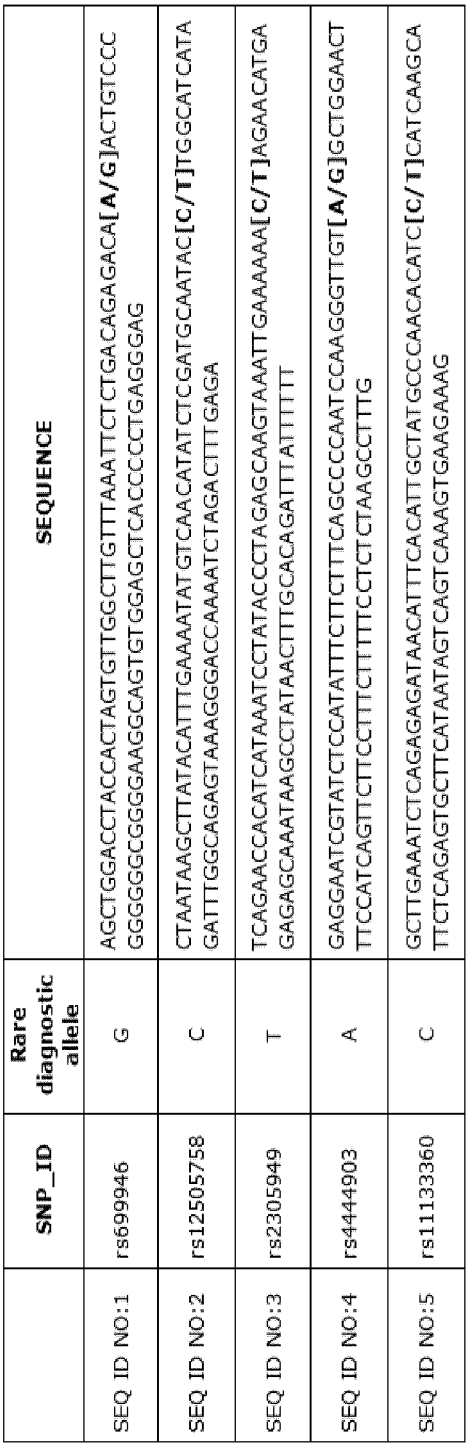

Study
TE seTE
95%−CI W(fixed)
BO17708 0.04 0.1031 0.04 [−0.16; 0.25] 37.6%
NO16966 0.25 0.1116 0.25 [0.03; 0.47] 32.0%
BO17704 0.28 0.1869 0.28 [−0.08; 0.65] 11.4%
BO17706 −0.10 0.2039 −0.10 [−0.50; 0.30] 9.6%
BO17705 0.37 0.2064 0.37 [−0.03; 0.78] 9.4%
Fixed effect model 0.16 [0.03; 0.28] 100%
Heterogeneity: I−squared=22%, tau−squared=0.0062, p=0.2746
−0.4 0 0.2 0.4 0.6
Log(HR)

Figure 14



	SNP_ID	Rare diagnostic allele	SEQUENCE
SEQ ID NO:1	rs699946	G	AGCTGGACCTACCACTAGTGTTGGCTTGTTTAAATTCTCTGACAGAGACA**[A/G]**ACTGTCCC GGGGGGCGGGGAAGGCAGTGTGGAGCTCACCCCCTGAGGGAG
SEQ ID NO:2	rs12505758	C	CTAATAAGCTTATACATTTGAAAATATGTCAACATATCTCGATGCAATAC**[C/T]**TGGCATCATA GATTTGGCAGAGTAAAGGGACCAAAATCTAGACTTTGAGA
SEQ ID NO:3	rs2305949	T	TCAGAACCACATCATAAATCCTATACCCTAGAGCAAGTAAATTGAAAAAA**[C/T]**AGAACATGA GAGAGCAAATAAGCCTATAACTTTGCACAGATTTATTTTTT
SEQ ID NO:4	rs4444903	A	GAGGAATCGTATCTCCATATTTCTTCTTTCAGCCCCAATCCAAGGGTTGT**[A/G]**GCTGGAACT TTCCATCAGTTCTTCCTTTCTTTTTCCTCTCTAAGCCTTTG
SEQ ID NO:5	rs11133360	C	GCTTGAAATCTCAGAGAGATAACATTTCACATTGCTATGCCCAACACATC**[C/T]**CATCAAGCA TTCTCAGAGTGCTTCATAATAGTCAGTCAAAGTGAAGAAAG