

eTable 4: Outcome of high vs. low normalized *AREG* expression according to molecular tumor characteristics by univariate Cox regression for overall and progression-free survival.

Parameter				Overall survival		Progression-free survival	
	<i>AREG</i> threshold value	<i>n</i> <i>AREG</i> high	<i>n</i> <i>AREG</i> low	HR [95% CI]	<i>p</i> value	HR [95% CI]	<i>p</i> value
<i>RAS</i> wild-type (<i>n</i> = 415)	Median	210	205	0.78 [0.63 – 0.96]	0.02	0.77 [0.63 – 0.94]	0.01
<i>RAS</i> mutated (<i>n</i> = 253)	Median	123	124	0.85 [0.65 – 1.10]	0.22	0.71 [0.55 – 0.93]	0.01
<i>BRAF</i> wild-type (<i>n</i> = 548)	Median	262	286	0.77 [0.64 – 0.92]	0.004	0.74 [0.62 – 0.87]	< 0.001
<i>BRAF</i> mutated (<i>n</i> = 51)	Median	23	28	0.88 [0.49 – 1.58]	0.66	0.54 [0.30 – 0.99]	0.05
<i>PIK3CA</i> wild-type (<i>n</i> = 613)	Median	309	304	0.80 [0.68 – 0.95]	0.01	0.71 [0.61 – 0.84]	< 0.001
<i>PIK3CA</i> mutated (<i>n</i> = 62)	Median	30	32	0.73 [0.42 – 1.26]	0.26	1.10 [0.66 – 1.84]	0.71
<i>EGFR</i> negative (<i>n</i> = 156)	Median	74	82	0.91 [0.65 – 1.29]	0.61	0.71 [0.51 – 0.98]	0.039
<i>EGFR</i> positive (<i>n</i> = 140)	Median	66	74	0.60 [0.41 – 0.86]	0.005	0.57 [0.40 – 0.81]	0.002
<i>RAS</i> wild-type (<i>n</i> = 415)	3rd quartile	121	294	0.76 [0.60 – 0.96]	0.021	0.86 [0.70 – 1.08]	0.19
<i>RAS</i> mutated (<i>n</i> = 247)	3rd quartile	47	200	0.79 [0.56 – 1.11]	0.17	0.70 [0.50 – 0.98]	0.04
<i>BRAF</i> wild-type (<i>n</i> = 548)	3rd quartile	137	411	0.75 [0.61 – 0.93]	0.009	0.80 [0.66 – 0.98]	0.03
<i>BRAF</i> mutated (<i>n</i> = 51)	3rd quartile	9	42	0.66 [0.30 – 1.43]	0.29	0.60 [0.29 – 1.25]	0.17
<i>PIK3CA</i> wild-type (<i>n</i> = 613)	3rd quartile	155	458	0.75 [0.62 – 0.92]	0.004	0.77 [0.64 – 0.93]	0.006
<i>PIK3CA</i> mutated (<i>n</i> = 62)	3rd quartile	15	47	0.89 [0.48 – 1.66]	0.71	1.10 [0.60 – 2.03]	0.76
<i>EGFR</i> negative (<i>n</i> = 156)	3rd quartile	34	122	0.82 [0.54 – 1.24]	0.35	0.78 [0.53 – 1.15]	0.21
<i>EGFR</i> positive (<i>n</i> = 140)	3rd quartile	33	107	0.62 [0.40 – 0.98]	0.039	0.54 [0.34 – 0.84]	0.006

Legend: HR = hazard ratio; 95% CI = 95% confidence interval; *AREG* = amphiregulin. *EGFR* positive tumors are defined as Neumann score > 22.5 and *EGFR* negative tumors as Neumann score < 22.5. Hazard ratios < 1.00 favor high and > 1.00 low *AREG* expression, respectively. *P* values < 0.05 are considered significant and displayed **bold**.