Updatedanalysisof *KRAS/NRAS* and *BRAF* mutationsinstudy 20050181 ofpanitumumab (pmab) plus FOLFIRI forsecond-linetreatment (tx) ofmetastaticcolorectalcancer (mCRC)

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Abstract:

Background: Previously, extended *RAS* analysisfromthisstudyshowed a trendtowardimprovementsin HR on OS and PFS withpmab + FOLFIRI vs FOLFIRI in WT *RAS* groupvs WT *KRAS* exon 2 group. Herewereportupdated *RAS* dataandnewanalysisby *BRAF* status.

Methods: Theprimaryobjectivewastoassessthetxeffectofpmab + FOLFIRI vs FOLFIRI on OS and PFS basedon *RAS/BRAF* mutationstatusintheprimaryanalysispopulation. BidirectionalSangersequencingwasusedtodetectmutationsin *KRAS* exons 3, 4 and *NRAS* exons 2, 3, 4, and *BRAF* exon 15 inpatients (pts) withknown WT *KRAS* exon 2 mCRC.

Results: Overall *RAS/BRAF* ascertainmentratewas 85% (n=1014/1186). 18% of WT *KRAS* exon 2 ptsharboredadditional *RAS*mutations (n=107/597). Theincidenceof *BRAF* mutationswas 8.3% (45/541). Efficacyisshown (table). Tx HR forptswith WT *RAS* was 0.81 (95% CI: 0.63, 1.03; *P*=0.08) for OS and 0.70 (95% CI: 0.54, 0.91; *P*=0.007) for PFS.

Conclusions: Improvementscontinuedtobeobservedinthetxeffectofpmab + FOLFIRI vs FOLFIRI on OS and PFS in WT *RAS* groupvs WT *KRAS* exon 2 groupinthisupdate. Ptswith MT *RAS* mCRCareunlikelytobenefitbytheadditionofpmabto FOLFIRI, similartoptswith MT *KRAS* exon 2 mCRC. *BRAF* mutationsappeartobeassociatedwithreduced OS amongptswithout *RAS*mutationsregardlessoftxarm.
Thesefindingssupport *RAS* testingtodeterminepotentiallyappropriateptswithmCRCforpmabtx.
Clinicaltrialinformation: **NCT00339183**.

	Pmab + FOLFIRI (N = 303)	**FOLFIRI (N = 294)**	**HR (95% CI)**
WT *RAS*,[a] n	208	213	
Median OS - mos	16.2	13.9	0.81
95% CI	14.5, 19.7	11.9, 16.0	0.63,1.03
Median PFS - mos	6.4	4.6	0.70
95% CI	5.5, 7.4	3.7, 5.6	0.54,0.91
MT *RAS*,[b] n	299	294	
Median OS - mos	11.8	11.1	0.91
95% CI	10.4, 13.1	10.2, 12.4	0.76, 1.10

	Pmab + FOLFIRI (N = 303)	FOLFIRI (N = 294)	HR (95% CI)
Median PFS - mos	4.8	4.0	0.86
95% CI	3.7, 5.5	3.6, 5.5	0.71, 1.05
WT *RAS*/WT *BRAF*[c]	186	190	
Median OS - mos	18.7	15.4	0.83
95% CI	15.7, 20.3	13.0, 17.9	0.64,1.07
Median PFS - mos	6.9	5.5	0.68
95% CI	5.8, 8.0	3.9, 5.9	0.51,0.90
WT *RAS*/MT *BRAF*[d]	22	23	
Median OS - mos	4.7	5.7	0.64
95% CI	2.8, 9.0	3.5, 7.3	0.32,1.28
Median PFS - mos	2.5	1.8	0.69
95% CI	1.7, 3.5	1.8, 3.1	0.32,1.49

[a] WT in *KRAS* and *NRAS*exons 2, 3, and 4.[b] MT inany *KRAS* or *NRAS* exon 2, 3, or 4. [c] WT forall *RAS* and *BRAF* exons. [d] WT forall *RAS* and MT *BRAF*exons.