events (AEs) were reported in 8/10 patients; none were serious. The most common AE was headache (n = 5). Six of 10 patients met the criteria for efficacy analysis. For Cohort 1 (n = 5), no patients had disease progression and 3/5 reported clinical benefit (best response: 3 reported pain reduction, 2 each reported improved mobility and function). In 9 of 12 study visits, ⩾50% of patients had a clinically meaningful improvement in worst pain (⩾2-point decrease) from baseline. Except for one patient at weeks 25 and 37, no other patient increased analgesic use from no/low (0−2 points) at baseline to strong opioids (⩾3 points) throughout the study. The one patient in Cohort 2 eligible for efficacy analysis, delayed a planned morbid surgery for at least 6 months.

Conclusions: Denosumab was well tolerated in these adolescent patients with GCTB. Reduced disease progression, delayed surgery, and clinical benefit were reported. Denosumab continues to be studied as a potential treatment for skeletally mature adolescents with GCTB.

Personalized Medicine

Sunday 25 September 2011, 09:00−10:50

33LBA LATE BREAKING ABSTRACT

Evaluation of Individual Codon 12 and 13 Mutant (MT) KRAS Alleles as Prognostic and Predictive Biomarkers of Response to Panitumumab (pmab) in Patients with Metastatic Colorectal Cancer (mCRC)

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Background: Pmab is a fully human monoclonal antibody targeting the epidermal growth factor receptor (EGFR). Significant improvement in progression-free survival (PFS) was observed in patients with wild-type (WT) *KRAS* mCRC receiving pmab + FOLFOX4 for 1st-line therapy (study 20050203; Identifier: NCT00364013; Sponsor: Amgen), pmab + FOLFIRI for 2nd-line therapy (study 20050181; Identifier: NCT00339183; Sponsor: Amgen), and pmab + best supportive care (BSC [study 20020408; Identifier: NCT00113763; Sponsor: Amgen]). Collectively, MT *KRAS* codon 12 and 13 alleles are established biomarkers for lack of response to anti-EGFR antibodies in mCRC. We evaluated the prognostic and predictive impact of individual codon 12 and 13 *KRAS* mutations in these three phase 3 studies.

Methods: Patients were randomized 1:1 to receive FOLFOX4, FOLFIRI, or BSC +/− pmab 6.0 mg/kg Q2W. The primary endpoint in studies 20050203 and 20020408 was PFS; overall survival (OS) was a secondary endpoint. In study 20050181, the co-primary endpoints were PFS and OS. *KRAS* status was determined using the Therascreen® *K-RAS* Mutation Kit (Qiagen) that detects the seven most common *KRAS* mutations in codons 12 and 13 (*KRAS* G12A, G12C, G12D, G12R, G12S, G12V, G13D).

Results: *KRAS* ascertainment rates were 93%, 91%, and 92% in studies 20050203, 20050181, and 20050408, respectively. MT *KRAS* codon 12 and 13 alleles were detected in 40% (440/1,096), 45% (486/1,083), and 43% (184/427) of tumors from patients in studies 20050203, 20050181, and 20020408, respectively. The distribution of MT *KRAS* alleles was conserved across studies, equally balanced between treatment arms, and consistent with published mCRC *KRAS* mutation analyses. Baseline demographic and clinical features were generally balanced in all MT *KRAS* allele subgroups. Across three studies, none of the individual MT *KRAS* alleles were consistently associated with PFS or OS outcomes in the treatment arms. Only in study 20050203 were two individual *KRAS* MT alleles significantly associated with outcomes: G12V was favorably and G13D was unfavorably associated with OS in the pmab-containing arm. Response rates were comparable across all MT *KRAS* allele subgroups within each of the 1st- and 2nd-line mCRC trials; no patients with MT *KRAS* mCRC responded to pmab therapy in study 20020408.

Conclusions: These retrospective analyses indicate that patients with mCRC whose tumors harbor MT *KRAS* codon 12 or 13 alleles are unlikely to benefit from panitumumab therapy. Therefore, only patients with WT *KRAS* tumors should be treated with panitumumab therapy.

Lung Cancer − Metastatic

Saturday 24 September 2011, 11:15−14:05

34LBA LATE BREAKING ABSTRACT

AVAPERL (MO22089): Final Efficacy Outcomes for Patients (pts) With Advanced Non-squamous Non-small Cell Lung Cancer (nsNSCLC) Randomised to Continuation Maintenance (mtc) with Bevacizumab (bev) or Bev + Pemetrexed (pem) After First-line (1L) Bev–cisplatin (cis)–pem Treatment (Tx)

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Background: 1L bev-based Tx followed by mtc bev offers clinical benefit over chemotherapy alone, as does 1L cis–pem followed by mtc pem. AVAPERL (NCT 00961415) is a randomized, multicenter, open-label phase III study investigating whether continuation mtc with bev+pem offers benefit over bev alone after 1L bev–cis–pem. AVAPERL is ongoing and sponsored by F. Hoffmann-La Roche Ltd.

Materials and Methods: Eligible pts with advanced/metastatic/recurrent nsNSCLC who achieved CR/PR/SD after 1L bev–cis–pem were randomized 1:1 to receive bev or bev+pem until disease progression (PD) or unacceptable toxicity. Primary endpoint was progression-free survival (PFS) from start of 1L Tx to 1st PD or death from any cause. Treatment difference in PFS was evaluated by stratified log-rank test; stratification factors were gender, smoking status and response after 1L Tx. Secondary efficacy endpoints included overall survival (OS), best overall response rate (ORR), duration of response, and duration of disease control. The total analysis population included all eligible patients. The mtc analysis population included all patients randomised to receive mtc Tx.

Results: Eighty-one sites in 11 countries enrolled 376 patients between 08/09 and 07/10. Of these, 253 pts (67%) were randomised: 125 (49%) to bev, and 128 (51%) to bev+pem. Baseline characteristics were well-balanced. Tx was well-tolerated (ECCO 2011, #9.112) and QoL did not deteriorate with mtc Tx (ECCO 2011, #9.076). Median follow-up for the mtc arms was 11 mo. Data are presented in Table 1.

Table 1

	Bev mtc n = 125	Bev+pem mtc n = 128	HR	p
mPFS* (mo) (95% CI)	6.6 (6.0−7.8)	10.2 (9.1–11.7)	0.50	<0.001
mOS (mo) (95% CI)	15.7 (14.3-NR)	NR§ (NR-NR)	0.75	0.23
Best ORR (%) (95% CI)	50 (40.9–59.1)	55.5 (46.4–64.3)	−	0.88
Median duration of response (mo) (95% CI)	5.7 (4.9−7.2)	9.2 (6.8–10.4)	0.53	0.006
Median duration of disease control (mo) (95% CI)	4.9 (3.9−5.7)	7.8 (6.8−9.7)	0.52	<0.001

*m = median. §NR = not reached.

Conclusions: Overall, 1L Tx with cis–pem–bev followed by mtc bev or bev+pem is well-tolerated. Continuation mtc with bev+pem results in the most pronounced mPFS (10.2 mo) and reduction in risk of progression (50%, HR = 0.50) observed in this setting of patients with nsNSCLC who achieve disease control.