LBA1 **Plenary Session**

Panitumumab (PAN) plus mFOLFOX6 versus bevacizumab (BEV) plus mFOLFOX6 as first-line treatment in patients with *RAS* wild-type (WT) metastatic colorectal cancer (mCRC): Results from the phase 3 PARADIGM trial.

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Background: PARADIGM is the first prospective trial to test the superiority of PAN vs. BEV in combination with standard doublet first-line chemotherapy for patients (pts) with *RAS* WT mCRC and left-sided primary tumors. **Methods:** This open-label, multicenter trial in Japan (NCT02394795) randomly selected pts with chemotherapy-naive *RAS* WT mCRC to PAN + mFOLFOX6 or BEV + mFOLFOX6. Overall survival (OS) as primary endpoint was hierarchically tested in patients with left-sided tumors, followed by those in the full-analysis set (FAS) population. Key secondary endpoints included progression-free survival (PFS), response rate (RR), and curative resection (R0) rate. **Results:** From May 2015 to June 2017, 823 pts were randomized; 12 did not receive protocol treatment and 9 were excluded due to major deviation of inclusion criteria. A total of 400 pts received PAN and 402 pts received BEV as FAS; 312 and 292 pts had left-sided primary tumors, respectively. OS was analyzed after 448 OS events in left-sided pts with a median follow-up of 61 months. PAN significantly improved OS vs. BEV in both populations: left-sided (HR, 0.82; 95.798% CI, 0.68-0.99, p = .031, which crossed the boundary of significance [0.042]), and FAS (HR, 0.84; 95% CI, 0.72-0.98; p = .030, with < 0.05 as the boundary). Although PFS was comparable between treatment groups, RR and R0 resection rates were higher with PAN compared with BEV (Table). HR for OS in the right-sided population was 1.09. No new safety signal was observed. **Conclusions:** PAN significantly improved OS vs. BEV in combination with mFOLFOX6 in pts with *RAS* WT and left-sided mCRC, establishing a standard first-line combination regimen for this population. Clinical trial information: NCT02394795. Research Sponsor: Japan Medical Affairs, Japan Oncology Business Unit, Takeda Pharmaceutical Company Ltd., Tokyo, Japan.

PARADIGM efficacy outcomes.

	PAN + mFOLFOX6	BEV + mFOLFOX6	HR (CI)[a]	*P*p value
Left-sided tumor population	**n=312**	**n=292**		
Median OS, mo	37.9 (34.1-42.6)	34.3 (30.9-40.3)	0.82 (0.68-0.99)	0.031
Median PFS, mo	13.7 (12.7-15.3)	13.2 (11.4-14.5)	0.98 (0.82-1.17)	
RR, %	80.2 (75.3-84.5)	68.6 (62.9-74.0)		
R0 resection, %	18.3 (14.1-23.0)	11.6 (8.2-15.9)		
FAS population	**n=400**	**n=402**		
Median OS, mo	36.2 (32.0-39.0)	31.3 (29.3-34.1)	0.84 (0.72-0.98)	0.030
Median PFS, mo	12.9 (11.3-13.6)	12.0 (11.3-13.5)	1.01 (0.87-1.18)	
RR, %	74.9 (70.3-79.1)	67.3 (62.4-71.9)		
R0 resection, %	16.5 (13.0-20.5)	10.9 (8.1-14.4)		