LBA44 **Pembrolizumab with or without chemotherapy vs chemotherapy in patients with advanced G/GEJ cancer (GC) including outcomes according to Microsatellite Instability-High (MSI-H) status in KEYNOTE-062**

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Background: KEYNOTE-062 (NCT02494583) was a randomized, study of 1L pembrolizumab (P) or pembro + chemo (P+C) vs chemo (C) in patients (pts) with PD-L1 combined positive score ≥1 (CPS ≥1), HER2-negative, advanced GC.

Methods: Eligible pts were randomized 1:1:1 to P 200 mg Q3W for up to 2 y, P+C (cisplatin 80 mg/m^2 + 5-FU 800 mg/m^2/d on d1-d5 Q3W [or capecitabine 1000 mg/m^2 BID on d1-d14 Q3W per local guideline]) or placebo Q3W + C. Primary endpoints were OS in CPS ≥1 and CPS ≥10 for P+C vs C and P vs C and PFS (RECIST v1.1; central review) in CPS ≥1 for P+C vs C. ORR (RECIST v1.1; central review) in CPS ≥1 for P+C vs C was the secondary endpoint. The final analysis cutoff date was 26 Mar 2019.

Results: 763 pts (281 with CPS ≥10) were randomized to P+C (257), P (256), or C (250) (Table). Median follow-up was 11.3 mo. P was noninferior to C for OS in CPS ≥1 per prespecified margins. P vs C prolonged OS in CPS ≥10 (median 17.4 vs 10.8 mo; HR 0.69; 95% CI 0.49-0.97) but wasn't tested per analysis plan. P+C vs C was not superior for OS in CPS ≥1 or CPS ≥10, with a favorable trend for P+C. In an exploratory analysis of pts with MSI-H tumors with CPS ≥1 (N = 50), median OS was not reached vs 8.5 mo for both P vs C (HR 0.29; 95% CI 0.11-0.81) and P+C vs C (HR 0.37; 95% CI 0.14-0.97). PFS was longer with P vs C (HR 0.72; 95% CI 0.31-1.68) and P+C vs C (HR 0.45; 95% CI 0.18-1.11). ORR was higher with P (57%) and P + C (65%) vs C (37%). Median DOR was 21.2 mo with P, not reached (P + C) vs 7.0 mo (C). Grade 3-5 drug-related AE rates were 17% (P), 73% (P+C), and 69% (C).

Conclusions: As 1L therapy for advanced GC, P was noninferior to C for OS in CPS ≥1 with clinically meaningful improvement for OS in CPS ≥10. P+C did not show superior OS and PFS in CPS ≥1 and OS in CPS ≥10. Clinical benefit was substantially enhanced in a small subset of pts with MSI-H tumors. The safety profile was more favorable for P vs C.

Clinical trial identification: NCT02494583.

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Table: LBA44

CPS ≥1 [a]Median, mo (95% CI)	P+C N = 257	C N = 250	P N = 256	C N = 250
OS[a]	12.5 (10.8-13.9)/ 11.1 (9.2-12.8)		10.6 (7.7-13.8)/11.1 (9.2-12.8)	
HR (95% CI)/ [b]99.2% CI	0.85 (0.70-1.03) P = 0.046		0.91 (0.74-1.10) 0.91[b] (0.69-1.18); NI margin = 1.2	
PFS[a]	6.9 (5.7-7.3)/ 6.4 (5.7-7.0)		2.0 (1.5-2.8)/6.4 (5.7-7.0)	
HR (95% CI)	0.84 (0.70-1.02); P = 0.039		1.66 (1.37-2.01)	
MSI-H	N = 17/N=19		N = 14/N=19	
OS[a]	Not reached (3.6-NR)/8.5 (5.3-20.8)		Not reached (10.7-NR)/8.5 (5.3-20.8)	
ORR, %	64.7/36.8		57.1/36.8	
PFS[a]	Not reached (3.6-NR)/6.6 (4.4-8.3)		11.2 (1.5-NR)/6.6 (4.4-8.3)	
DOR, median, mo (range)	NR (1.6+ to 34.5+)/7.0 (2.0-30.4+)		21.2 (1.4+ to 33.6+)/7.0 (2.0-30.4+)	

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