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MEETING SUMMARY

ASCO 2020, San Francisco, USA

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HIGHLIGHTS ON UPPER GI

January 2020

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This content is supported by an Independent Educational Grant from Bayer.

BACKGROUND ON MAINTENANCE THERAPY

- **Maintenance therapy** is one strategy to improve and extend the duration of tumour responses/disease control, PFS, OS and QOL in the 1L setting without additive toxicity¹
- **Maintenance therapy** has been shown to extend the duration of antitumour benefit following standard 1L induction treatment in patients with non-small-cell lung cancer and colorectal cancer¹
- **The role of maintenance therapy in GC/GEJC** is not yet established. However observational and retrospective studies reported to date have shown that maintenance treatment with fluoropyrimidines is feasible and may improve PFS compared with observation¹

1. Moehler M, et al. Future Oncol 2018;15(6):567-77

1L, first line; GC; gastric cancer; GEJC, Gastroesophageal junction cancer; OS, overall survival; PFS, progression-free survival; QOL, quality of life

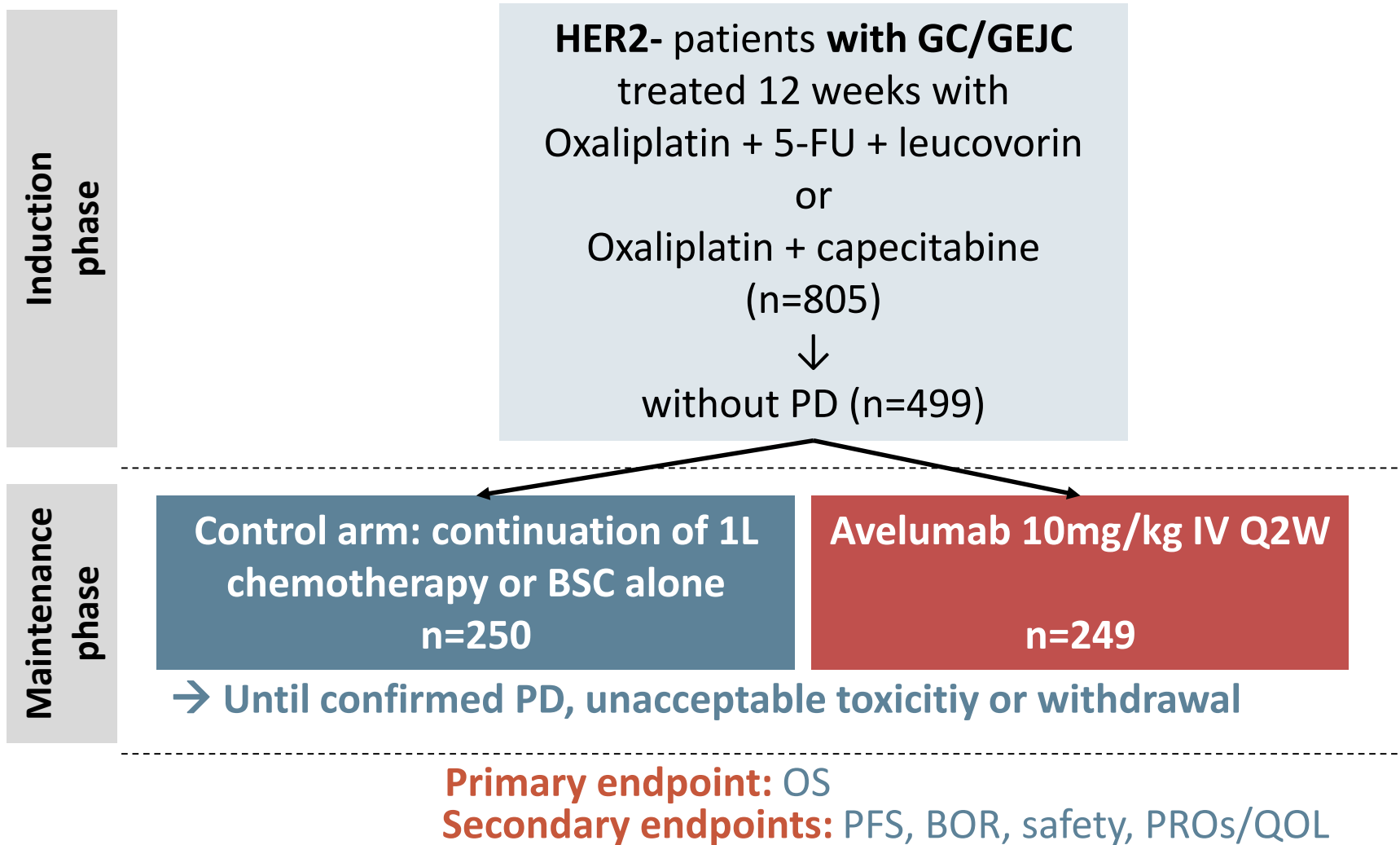
**RESULTS OF THE JAVELIN
GASTRIC 100 PHASE 3 TRIAL:
AVELUMAB MAINTENANCE FOLLOWING
FIRST-LINE (1L) CHEMOTHERAPY (CTX)
VS CONTINUATION OF CTX FOR
HER2-ADVANCED GASTRIC OR
GASTROESOPHAGEAL JUNCTION
CANCER (GC/GEJC)**

Moehler MH, et al. ASCO GI 2020, abst #278

JAVELIN GASTRIC 100 STUDY: DESIGN

- **Design:** International, open-label, phase 3 trial
- **ClinicalTrials.gov Identifier:** NCT02625610
- **The primary objective:** to demonstrate that avelumab maintenance therapy is superior to continuation of 1L chemotherapy with regard to OS measured from randomisation, that is, the start of maintenance treatment, in all randomised patients or in patients with PD-L1+ tumours

JAVELIN GASTRIC 100 STUDY: DESIGN



JAVELIN GASTRIC 100 STUDY: PRIMARY ENDPOINT OS RESULTS

Arms (in all population)	Chemotherapy (n=250)	Avelumab (n=249)	HR (95% CI)	P value (1-sided)
Events (n)	196	185		
Median OS (95% CI), months	10.9 (9.6-12.4)	10.4 (9.1-12.0)	0.91 (0.74-1.11)	0.1779

Arms (in PD-L1+ population*)	Chemotherapy (n=24)	Avelumab (n=30)	HR (95% CI)	P value (1-sided)
Events (n)	15	19		
Median OS (95% CI), months	17.7 (9.6-NR)	16.2 (8.2-NR)	1.13 (0.57-2.23)	0.6352

*PD-L1+ cutoff : ≥1% of tumour cells

JAVELIN GASTRIC 100 STUDY: SECONDARY ENDPOINTS PFS RESULTS

Arms (in all population)	Chemotherapy (n=250)	Avelumab (n=249)	HR (95% CI)	P value (1-sided)
Events (n)	188	189		
Median PFS (95% CI), months	4.4 (4.0-5.5)	3.2 (2.8-4.1)	1.04 (0.85-1.28)	0.6433

Arms (in PD-L1+ population*)	Chemotherapy (n=24)	Avelumab (n=30)	HR (95% CI)	P value (1-sided)
Events (n)	16	19		
Median PFS (95% CI), months	9.7 (2.8-12.5)	4.1 (1.6-16.0)	1.04 (0.53-2.02)	0.9147

*PD-L1+ cutoff : ≥1% of tumour cells

CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; PD-L1, Programmed death-ligand 1

JAVELIN GASTRIC 100 STUDY: SECONDARY ENDPOINTS SAFETY RESULTS



Safety (in all population)	Chemotherapy (n=238)	Avelumab (n=243)
AE (related or unrelated), % (n)	89.9 (214)	91.8 (223)
Grade ≥3	53.8 (128)	54.3 (132)
TRAE, % (n)	77.3 (184)	61.3 (149)
Grade ≥3	32.8 (78)	12.8 (31)
TRAE leading to permanent discontinuation, % (n)	27.3 (65)	10.3 (25)

**EVALUATING MAINTENANCE
THERAPIES IN ADVANCED
OESOPHAGO-GASTRIC
ADENOCARCINOMA (OGA): INTERIM
ANALYSIS AND BIOMARKER RESULTS
FROM THE PLATFORM STUDY**

Cunningham D, et al. ASCO GI 2020, abst #282

PLATFORM STUDY: DESIGN

- **PLATFORM** (ClinicalTrials.gov Identifier: NCT02678182) is a prospective, open-label, multi-centre, randomised phase II study
- **Objective:** to assess the efficacy of several maintenance therapies following completion of standard first-line chemotherapy in patients with locally advanced or metastatic HER-2 positive or HER-2 negative OGA
- **Primary endpoint:** PFS (time frame 5 years)
- **Secondary endpoints:** PFR, OS, ORR by RECIST 1.1, AEs assessed by CTCAE v4.0 (time frame 5 years)
- **Results presented** = interim analysis of 61 patients/arm and evaluable at 12 weeks

PLATFORM STUDY: INTERIM ANALYSIS SNAPSHOT

- **Data lock** = 7 January 2020

HER2- patients
treated with platinum +
fluoropyrimidine

Arm A

A1: surveillance n=92

A2: capecitabine n=99

A3: durvalumab n=100

A4: rucaparib n=38

A5: capecitabine + ramucirumab n=3

HER2+ patients
cisplatin in combination
with either capecitabine
or 5-FU (CX or CF) plus
trastuzumab
chemotherapy

Arm B

B1: Trastuzumab n=36

B2: Trastuzumab + durvalumab

PLATFORM STUDY: INTERIM ANALYSIS – PFR AT 12 WEEKS

- **Data lock** = 7 January 2020

Arms	A1: surveillance (n=61)	A2: Capecitabine (n=61)	A3: Durvalumab n=61
PFR at 12 weeks	30 (49%)	34 (56%)	29 (48%)
PFR compared to A1 (95% CI)	Control	+6.6% (-8.3, +21.4%)	-1.6 (-16.5, +13.3%)
CR	0 (0%)	0 (0%)	0 (0%)
PR	0 (0%)	0 (0%)	3 (5%)
SD	30 (49%)	34 (56%)	26 (43%)
PD	28 (46%)	25 (41%)	31 (51%)
Clinical PD	3 (5%)	2 (3%)	1 (2%)

PLATFORM STUDY: INTERIM ANALYSIS – PFR AT 12 WEEKS BY PD-L1 STATUS AND TMB

- **Data lock** = 7 January 2020

Arm	A1: surveillance (n=44)		A3: Durvalumab (n=38)	
PD-L1 status	TIC ≥ 1 n=28	TIC ≥ 10 n=7	TIC ≥ 1 n=22	TIC ≥ 10 n=4
PFR	15 (54%)	3 (43%)	14 (64%)	4 (100%)
PD	13 (46%)	4 (57%)	8 (36%)	0 (0%)

Arm	A1: surveillance (n=37)			A3: Durvalumab (n=36)		
TMB*	Low n=14	Medium n=9	High n=14	Low n=11	Medium n=15	High n=10
PFR	9 (64%)	2 (22%)	8 (57%)	7 (64%)	6 (40%)	8 (80%)
PD	5 (36%)	7 (78%)	6 (43%)	4 (36%)	9 (60%)	2 (20%)

*TMB: low: 1.0-4.3; medium: >4.3-8.5; high: >8.5-79

PD, progressive disease; PD-L1, Programmed death-ligand 1; PFR, progression-free rate; TIC, tumour-associated immune cell score; TMB, tumour mutational burden

PLATFORM STUDY: INTERIM ANALYSIS – GRADE ≥ 3 TRAEs

- **Data lock** = 7 January 2020

Arms	A1: surveillance (n=61)	A2: Capecitabine (n=61)	A3: Durvalumab n=61
Grade 3	0 (0%)	8 (13%)	7 (11%)
Grade 4	0 (0%)	0 (0%)	2 (3%)
Grade 5	0 (0%)	0 (0%)	0 (0%)

CONCLUSIONS

- **JAVELIN study:**
 - Javelin study's primary objective not met (all and PD-L1+ population)
 - Avelumab showed favourable safety profile compared to continued chemotherapy
- **PLATFORM study:**
 - interim analysis did not meet its primary endpoint in maintenance capecitabine or durvalumab compared to surveillance in advanced OGA
- **Impact of these results:**
 - Current standard of care remains unchanged in GC/GEJC:
 - 1L: chemotherapy with 5-FU + platinum¹
 - 2L: being paclitaxel + ramucirumab¹
- Further analyses of these 2 studies are expected and some patient subsets might be found with potential benefit for further investigations

1. DT Le, et al. Clin Colorectal Cancer. 2019, pii: S1533-0028(19)30445-1

1L, first line; 2L, second line; 5-FU, fluorouracil; PD-L1, Programmed death-ligand 1; OGA, oesophago-gastric adenocarcinoma; GC, gastric cancer; GEJC, Gastroesophageal junction cancer

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