

## Supplementary file

Supplemental Table 1, Supplemental Figure 1

**Title:** A phase II study of FOLFIRI plus ziv-aflibercept after trifluridine/tipiracil plus bevacizumab in patients with metastatic colorectal cancer: WJOG 11018G

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### **Supplemental Figure legends**

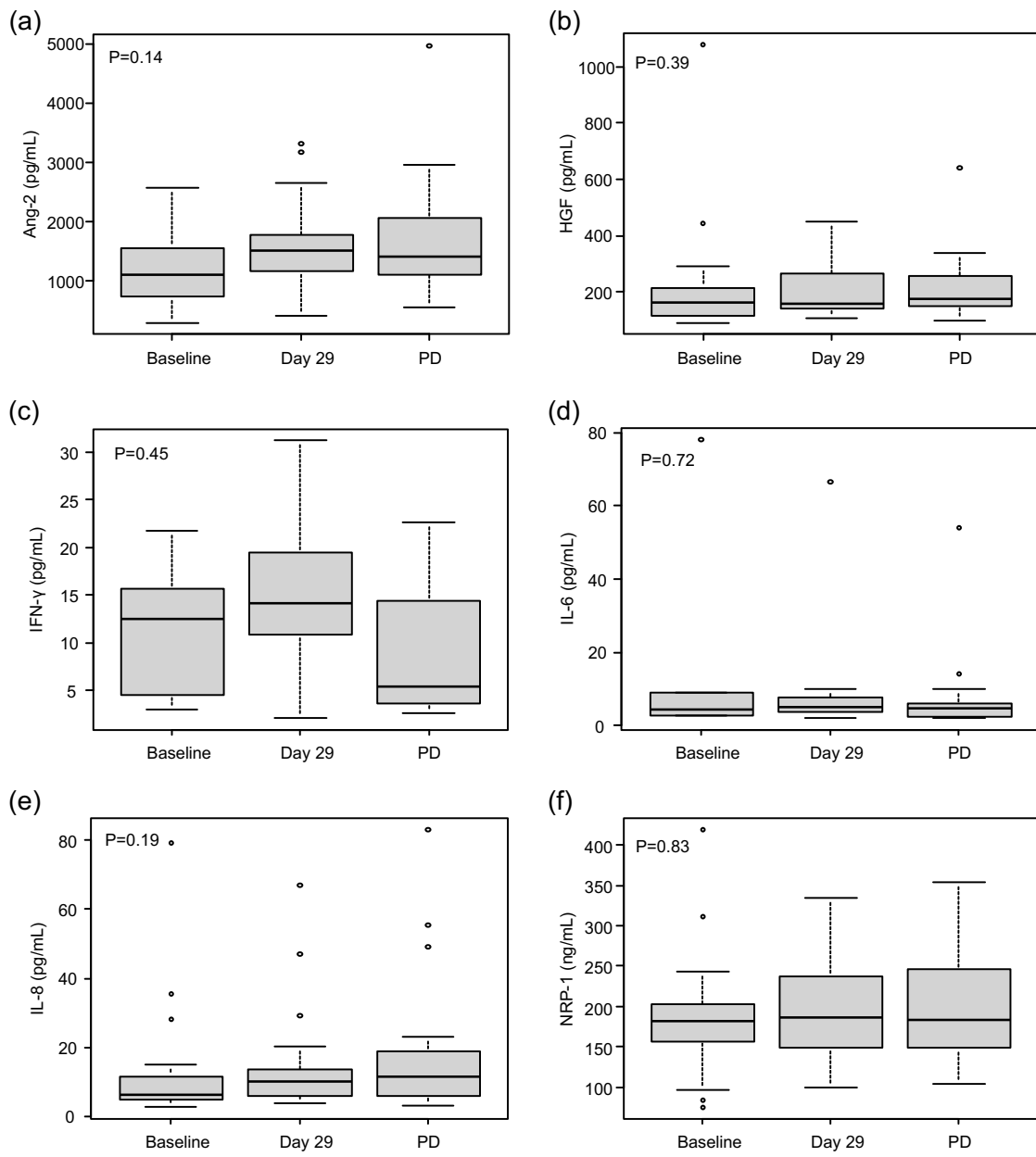
Supplemental Figure 1-1 and 1-2. Plasma biomarker dynamics at baseline, day 29, and PD. Box plots indicate median, quartile, and maximum/minimum values. Ang, angiopoietin-2; HGF, hepatocyte growth factor; PlGF, placental growth factor; VEGF, vascular endothelial growth factor; OPN, osteopontin; NRP-1, neuropilin-1; IL-8, Interleukin-8; TIMP-1, tissue inhibitor of matrix metalloproteinases-1; TSP-2, thrombospondin-2; sICAM, soluble intercellular adhesion molecule; sVCAM, soluble vascular cell adhesion molecule.

**Supplemental Table 1.** Biomarker analysis, overall response rate (ORR), and disease control rate (DCR)

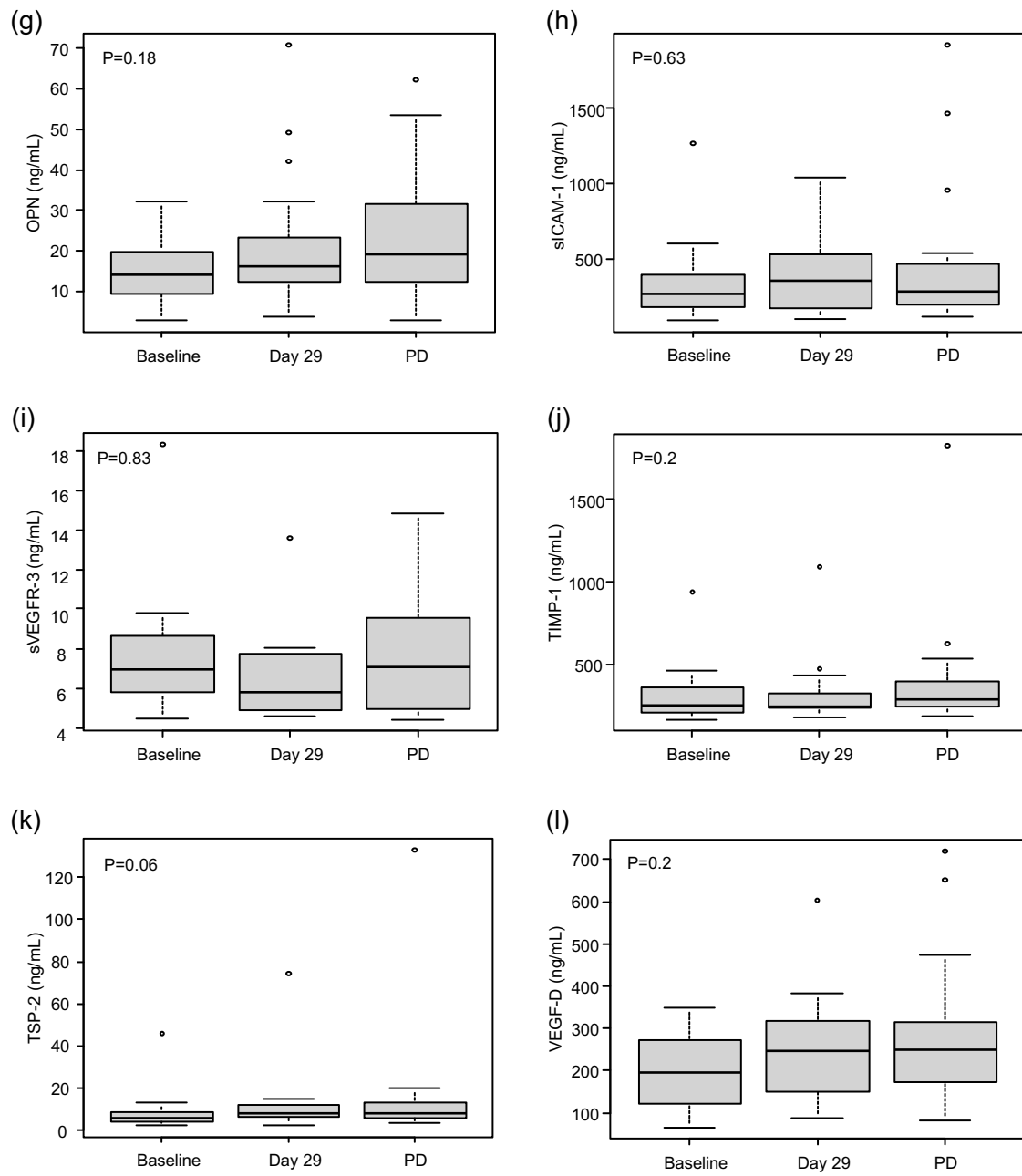
Factor	Category	Patients (n)	ORR (%) (95% CI)	P	DCR (%) (95% CI)	P
Ang-2 (median: 1100 pg/mL)	Low	11	9.1 (0.2–41.3)	1.00	72.7 (39.0–94.0)	0.41
	High	14	7.1 (0.2–33.9)		50.0 (23.0–77.0)	
HGF (median: 160 pg/mL)	Low	12	8.3 (0.2–38.5)	1.00	58.3 (27.7–84.8)	1.00
	High	13	7.7 (0.2–36.0)		61.5 (31.6–86.1)	
PlGF (median: 15.5 pg/mL)	Low	12	8.3 (0.2–38.5)	1.00	66.7 (34.9–90.1)	0.69
	High	13	7.7 (0.2–36.0)		53.8 (25.1–80.8)	
VEGF-D (median: 192.0 pg/mL)	Low	12	8.3 (0.2–38.5)	1.00	58.3 (27.7–84.8)	1.00
	High	13	7.7 (0.2–36.0)		61.5 (31.6–86.1)	
OPN (median: 14000 pg/mL)	Low	12	16.7 (2.1–48.4)	0.22	66.7 (34.9–90.1)	0.69
	High	13	0.0 (0.0–24.7)		53.8 (25.1–80.8)	
NRP-1 (median: 182000 pg/mL)	Low	12	8.3 (0.2–38.5)	1.00	50.0 (21.1–78.9)	0.43
	High	13	7.7 (0.2–36.0)		69.2 (38.6–90.9)	
VEGFR2 (median: 5320 pg/mL)	Low	12	0.0 (0.0–26.5)	0.48	50.0 (21.1–78.9)	0.43
	High	13	15.4 (1.9–45.4)		69.2 (38.6–90.9)	
IL-8 (median: 6.2 pg/mL)	Low	12	16.7 (2.1–48.4)	0.22	66.7 (34.9–90.1)	0.69
	High	13	0.0 (0.0–24.7)		53.8 (25.1–80.8)	
TIMP-1 (median: 254000 pg/mL)	Low	12	8.3 (0.2–38.5)	1.00	75 (42.8–94.5)	0.23
	High	13	7.7 (0.2–36.0)		46.2 (14.2–74.9)	
TSP-2 (median: 5760 pg/mL)	Low	12	8.3 (0.2–38.5)	1.00	50.0 (21.1–78.9)	0.43

	High	13	7.7 (0.2–36.0)		69.2 (38.6–90.9)	
sICAM-1 (median: 269000 pg/mL)	Low	12	16.7 (21.–48.4)	0.22	58.3 (27.7–84.8)	1.00
	High	13	0.0 (0.0–24.7)		61.5 (31.6–86.1)	
sVCAM-1 (median: 1140000 pg/mL)	Low	12	16.7 (21.–48.4)	0.22	58.3 (27.7–84.8)	1.00
	High	13	0.0 (0.0–24.7)		61.5 (31.6–86.1)	

Ang, angiopoietin-2; HGF, hepatocyte growth factor; PlGF, placental growth factor; VEGF, vascular endothelial growth factor; OPN, osteopontin; NRP-1, neuropilin-1; IL-8, Interleukin-8; TIMP-1, tissue inhibitor of matrix metalloproteinases-1; TSP-2, thrombospondin-2; sICAM, soluble intercellular adhesion molecule; sVCAM, soluble vascular cell adhesion molecule.



Supplemental Fig. 1-1



Supplemental Fig. 1-2