SUPPLEMENTARY TABLES

Supplementary Table 1. Treatment-emergent grade 3/4 adverse events in the safety population (n=116)

Adverse Event, n (%)	MEDI3617 monotherapy total (n=42)	MEDI3617 + bevacizumab Q3W escalation total (n=16)	MEDI3617 + bevacizumab Q2W total (n=38)	MEDI3617 + paclitaxel total (n=13)	MEDI3617 + carboplatin/ paclitaxel total (n=7)
Any grade ≥3 adverse event (no. patients)	21 (50)	8 (50)	22 (57)	5 (39)	5 (71)
Pleural effusion	3 (7)	1 (6)	0	0	0
Small intestinal obstruction	3 (7)	0	1 (3)	0	0
Hypertension	2 (5)	5 (31)	2 (5)	0	0
Fatigue	2 (5)	2 (13)	0	0	1 (14)
Hypokalemia	2 (5)	0	1 (3)	0	0
Dyspnea	2 (5)	0	1 (3)	0	0
Decreased appetite	2 (5)	0	0	0	1 (14)
Weight increased	2 (5)	0	0	0	0
Back pain	2 (5)	0	0	0	0
Pulmonary embolism	2 (5)	0	0	0	0
Myalgia	1 (2)	1 (6)	0	0	0
Pain in extremity	1 (2)	1 (6)	0	0	0
Vomiting	1 (2)	0	1 (3)	1 (8)	0
Pneumonia	1 (2)	0	1 (3)	1 (8)	0
Peripheral edema	1 (2)	0	1 (3)	1 (8)	0
Abdominal pain	1 (2)	0	1 (3)	0	0
Abdominal pain upper	1 (2)	0	0	0	0
Dehydration	1 (2)	0	0	0	1 (14)
Anemia	1 (2)	0	0	1 (8)	0
Neutropenia	1 (2)	0	0	0	3 (43)

Groin pain	1 (2)	0	0	0	0
Ascites	1 (2)	0	0	0	0
Edema	1 (2)	0	0	0	0
Abscess limb	1 (2)	0	0	0	0
Pneumonia	1 (2)	0	1 (3)	1 (8)	0
Blood alkaline phosphatase increased	1 (2)	0	0	0	0
Blood creatinine increased	1 (2)	0	0	0	0
Gamma glutamyltransferase increased	1 (2)	0	0	0	0
White blood cell count decreased	1 (2)	0	0	0	0
Dehydration	1 (2)	0	0	0	1 (14)
Hyperkalemia	1 (2)	0	0	0	0
Posterior reversible encephalopathy	1 (2)	0	0	0	0
Dysuria	1 (2)	0	0	0	0
Urinary tract obstruction	1 (2)	0	0	0	0
Pelvic pain	1 (2)	0	0	0	0
Dysphonia	1 (2)	0	0	0	0
Respiratory failure	1 (2)	0	0	0	0
Lymphodema	1 (2)	0	0	0	0
Hyponatremia	0	1 (6)	1 (3)	0	1 (14)
Hypophosphatemia	0	1 (6)	0	0	0
Osteomyelitis	0	1 (6)	0	0	0
Tooth infection	0	1 (6)	0	0	0
Aspartate aminotransferase	0	1 (6)	0	0	0

increased					
Blood potassium increased	0	1 (6)	0	0	0
Failure to thrive	0	1 (6)	0	0	0
Hyperuricemia	0	1 (6)	0	0	0
Muscular weakness	0	1 (6)	0	0	0
Leukocytosis	0	1 (6)	0	0	0
Nausea	0	0	1 (3)	1 (8)	0
Glioblastoma	0	0	3 (8)	0	0
Aphasia	0	0	2 (5)	0	0
Hemiparesis	0	0	3 (8)	0	0
Seizure	0	0	2 (5)	0	0
Proteinuria	0	0	2 (5)	0	0
Female genital tract fistula	0	0	2 (5)	0	0
Diarrhea	0	0	1 (3)	0	0
Dysphagia	0	0	1 (3)	0	0
Intestinal obstruction	0	0	1 (3)	0	0
Acute pancreatitis	0	0	1 (3)	0	0
Small intestinal obstruction	0	0	1 (3)	0	0
Asthenia	0	0	1 (3)	0	0
Medical device pain	0	0	1 (3)	0	0
Meningitis	0	0	1 (3)	0	0
Limb injury	0	0	1 (3)	0	0
Ataxia	0	0	1 (3)	0	0
Cognitive disorder	0	0	1 (3)	0	0
Headache	0	0	1 (3)	0	0
Memory impairment	0	0	1 (3)	0	0
Peripheral neuropathy	0	0	1 (3)	0	0
Urinary incontinence	0	0	1 (3)	0	0
Scrotal edema	0	0	1 (3)	0	0

Chronic obstructive pulmonary disease	0	0	1 (3)	0	0
Pneumothorax	0	0	1 (3)	0	0
Insomnia	0	0	1 (3)	0	0
Cardiac arrest	0	0	0	1 (8)	0
Urinary tract infection	0	0	0	1 (8)	0
Decreased ejection fraction	0	0	0	1 (8)	0
Troponin increased	0	0	0	1 (8)	0
Diabetes mellitus	0	0	0	1 (8)	0
Dizziness	0	0	0	1 (8)	0
Syncope	0	0	0	1 (8)	0
Confusional state	0	0	0	1 (8)	0
Acute respiratory failure	0	0	0	1 (8)	0
Pneumonitis	0	0	0	1 (8)	0
Hematoma	0	0	0	1 (8)	0
Nephrotic syndrome	0	0	0	0	1 (14)
Infusion-related reaction	0	0	0	0	1 (14)
Anaphylactic reaction	0	0	0	0	1 (14)
Drug hypersensitivity	0	0	0	0	1 (14)
Leukopenia	0	0	0	0	1 (14)

Supplementary Table 2. MEDI3617 pharmacokinetic parameters*

Cohort	$t_{½}$ (day)	C_{max} □g/mL	$AUC_{0–last}$ (day·□g/mL)	$AUC_{0–14d}$ (day·□g/mL)	$AUC_{0–inf}$ (day·□g/mL)	CL (mL/day)
Single-agent MEDI3617 Q3W						
5 mg	0.585 (NA)	1.39 (0.254)	1.3 (0.429)	1.79 (NA)	1.79 (NA)	2790 (NA)
10 mg	NA (NA)	2.44 (NA)	2.2 (NA)	NA (NA)	NA (NA)	NA (NA)
20 mg	1.26 (NA)	6.63 (3.48)	11.9 (11.8)	8.13 (NA)	8.12 (NA)	2460 (NA)
100 mg	5.86 (NA)	50.2 (28.8)	171 (69)	203 (NA)	269 (NA)	423 (NA)
300 mg	5.98 (3.09)	82.4 (2.68)	438 (204)	402 (130)	529 (269)	679 (345)
1000 mg	7.68 (NA)	239 (79.5)	2610 (1570)	1560 (NA)	2150 (NA)	465 (NA)
1500 mg	7.79 (NA)	785 (189)	3650 (2600)	2930 (NA)	4230 (NA)	355 (NA)
OC expansion 1000 mg	10.4 (3.15)	336 (62.2)	2610 (891)	1990 (637)	3280 (1410)	352 (136)
OC expansion 1500 mg	9.03 (NA)	346 (NA)	2160 (NA)	1710 (NA)	2490 (NA)	603 (NA)
MEDI3617 plus bevacizumab						
100 mg Q3W	3.59 (0.983)	30.4 (26.8)	101 (48.8)	101 (51.5)	110 (58.1)	1060 (426)
300 mg Q3W	9.67 (3.35)	55.3 (12.6)	473 (223)	380 (161)	628 (376)	614 (363)
1000 mg Q3W	NA (NA)	235 (90.5)	2280 (529)	NA (NA)	NA (NA)	NA (NA)
1500 mg Q3W	12.3 (NA)	348 (54.6)	2710 (1070)	2240 (NA)	3920 (NA)	388 (NA)

60 mg Q2W	3.9 (2.69)	44.5 (39.3)	94.7 (48.7)	94.8 (48.7)	104 (61)	797 (499)
200 mg Q2W	5.12 (0.541)	47.5 (23.3)	216 (61.8)	216 (61.5)	252 (83.2)	847 (237)
600 mg Q2W	8.23 (NA)	116 (35.1)	805 (292)	845 (NA)	1200 (NA)	501 (NA)
1000 mg Q2W	10.2 (NA)	275 (86.2)	2310 (941)	2870 (NA)	4630 (NA)	216 (NA)
Glioma expansion 1000 mg Q2W	NA (NA)	320 (170)	2590 (1920)	NA (NA)	NA (NA)	NA (NA)
MEDI3617 plus paclitaxel						
600 mg Q2W	6.96 (1.59)	114 (22.5)	551 (331)	638 (62.6)	849 (163)	727 (157)
1000 mg Q2W	9.34 (57.4)	209 (57.4)	1460 (484)	1830 (NA)	2810 (NA)	356 (NA)
MEDI3617 plus carboplatin plus paclitaxel						
1000 mg Q3W	15.1 (NA)	200 (25.8)	1240 (882)	1230 (NA)	2240 (NA)	446 (NA)
1500 mg Q3W	11.1 (NA)	585 (491)	2890 (257)	2300 (NA)	3560 (NA)	424 (NA)

*Values are mean (SD). $AUC_{0\text{-last}}$, area under the plasma concentration-time curve from time 0 to the time of the last quantifiable concentration; $AUC_{0\text{-14d}}$, area under the plasma concentration-time curve from time 0 to day 14 post-dose; $AUC_{0\text{-inf}}$, area under the plasma concentration time curve from time 0 to infinity; CL, systemic clearance; C_{max}, maximum observed serum concentration; N/A not applicable; Q2W, every 2 weeks; Q3W, every 3 weeks; SD, standard deviation; $t_{½}$, half-life.

Supplementary Table 3. Treatment outcome: objective response and progression-free survival, by cohort

	MEDI3617 monotherapy		**MEDI3617 plus bevacizumab**			**MEDI3617 plus chemotherapy**	
Response, n (%)	**Escalation (n=25)**	**Expansion in ovarian cancer (n=17)**	**Escalation Q3W (n=16)**	**Escalation Q2W (n=27)**	**Expansion Q2W in recurrent malignant glioma (n=11)**	**Paclitaxel (n=13)**	**Carboplatin plus paclitaxel (n=7)**
CR + PR	0	1 (6)	1 (6)	2 (7)	0	2 (15)	0
95% CI	(0, 14)	(0, 29)	(0, 30)	(1, 24)	(0, 29)	(2, 45)	(0, 41)
SD	13 (52)	5 (30)	11 (69)	10 (37)	2 (18)	4 (31)	3 (43)
PD	11 (44)	9 (53)	2 (13)	11 (41)	6 (55)	4 (31)	3 (43)
95% CI	(31, 72)	(14, 62)	(48, 93)	(26, 65)	(2, 52)	(19, 75)	(10, 82)
Median PFS, months	1.4	1.4	11.4	2.0	1.4	3.5	NA
95% CI	1.2, 2.6	1.1, 4.1	3.1, NA	1.6, 4.4	0.5, 1.4	1.7, NA	0, NA

CI, confidence interval; CR, complete response; DOR, duration of response; NA, not applicable; OR, objective response; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TTP, time to progression; TTR, time to response.