supplementary materials

supplementary methods

Approval was obtained from relevant regulatory authorities and local ethics committees at all participating sites. Informed consent was obtained from each patient before any study-related procedure. Adverse events were collected as defined by the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.

dose escalation

Intra-patient dose escalation was not permitted in the dose-escalation cohorts. If a dose-limiting toxicity (DLT) was observed in cycle 1 in a given cohort, dose escalation for subsequent cohorts was done by modified Fibonacci sequence, escalating by 50%, and then 33%, of the previous dose. DLTs were defined as any of the following events (per CTCAE version 3.0) occurring at any time during the study: any grade ≥3 toxicity (excluding sub-optimally treated nausea, vomiting, and diarrhea); grade 3 hyperglycemia following a fast of 8 h; any grade 4 hyperglycemia; grade 4 neutropenia lasting ≥3 days; absolute neutrophil count <1000/mm³ with fever ≥38°C; and grade 4 thrombocytopenia. Dose escalation was stopped if two or more of six patients experienced a DLT in cycle 1.

Dosing was allowed to continue at the next lower level if a patient experienced a non-hematologic DLT (excluding hyperglycemia) and if subjective or objective clinical benefit was observed, following consultation between the investigator and sponsor.

eligibility criteria

Other eligibility criteria included: adequate bone marrow, hepatic, and renal function; at least one measurable lesion or evaluable disease as defined by modified Response Evaluation
Criteria in Solid Tumors version 1.1 for patients with solid tumors; and Eastern Cooperative Oncology Group performance status of 0, 1, or 2. Patients with any subtype of non-Hodgkin’s lymphoma were eligible in the maximum tolerated dose (MTD) expansion phase. Patients with solid tumors in the MTD expansion phase had to have one of the following solid-tumor types: breast cancer (all subtypes), endometrial cancer, ovarian cancer (clear-cell and endometrioid types only), gastric cancer, or genitourinary transitional-cell carcinoma. Eight of the 24 solid-tumor patients were required to have a tumor \textit{PIK3CA} mutation in order to ensure assessment of copanlisib activity in the setting of phosphatidylinositol 3-kinase pathway activation. Patients in the diabetic cohort were required to have a current diagnosis of type 2 diabetes mellitus and be receiving anti-diabetic medication.

\textbf{exclusion criteria}

Key exclusion criteria were: current diagnosis of type 1 or 2 diabetes mellitus or fasting plasma glucose level $>125$ mg/dl at screening (except for patients in the diabetic cohort), or hemoglobin A1c $\geq 7\%$; use of systemic corticosteroids; uncontrolled hypertension; use of St John’s Wort or strong inducers or inhibitors of CYP3A4; primary brain or spinal tumors; or lymphoma involvement.

\textbf{assessments}

Screening included baseline demographics, safety, laboratory tests, urinalysis, and disease assessment by computed tomography or magnetic resonance imaging. During treatment, tumor assessments were performed within 1 week before day 1 of every odd-numbered cycle. Dipstick testing for urine ketones was performed post-dose on cycle 1, day 1. Serum samples were analyzed for ketones pre-dose, and at 3 and 8 h after the start of copanlisib infusion, on cycle 1, day 1. Hemoglobin A1c values were measured at odd-numbered cycles. Plasma and capillary blood samples were measured for glucose using automated chemistry panels and
portable glucometers, respectively. Safety evaluations included: physical examination; 12-lead electrocardiogram; echocardiography or multigated acquisition scan; vital signs; adverse events; and concomitant medications. Safety was assessed up to 30 days following the last dose of copanlisib.

Elevations in blood pressure were expected following copanlisib infusion based on preclinical data in laboratory animals, which observed dose-dependent peripheral vasoconstriction and elevation of blood pressure following intravenous administration of copanlisib (Bayer, data on file). Thus, blood pressure was monitored before, and at numerous intervals after, the start of infusion on day 1, at 0.5, 1, 1.5, 2, 3, 5, 8, 11, 25, and 49 h. For subsequent cycles, blood pressure was monitored before and 1 h after the end of the infusion. Hypertension was to be managed at the treating physician’s discretion.

Serial plasma samples for single-dose and steady-state pharmacokinetic evaluation of copanlisib were collected on days 1 and 15, respectively, of cycle 1, at 0, 0.5, 1, 1.5, 2, 3, 5, 8, 11, 25, and 49 h after the start of copanlisib infusion. A limited number of samples after multiple-dose administration was collected on cycle 3, day 15 from patients in the MTD expansion phase. Copanlisib plasma concentrations were determined after protein precipitation followed by separation employing liquid chromatography coupled with tandem mass spectrometry. The nominal calibration ranges for copanlisib were 0.5 µg/l (lower limit of quantitation) to 265 µg/l (upper limit of quantitation), and 2 µg/l (lower limit of quantitation) to 1057 µg/l (upper limit of quantitation).

For $[^{18}\text{F}]-\text{fluorodeoxyglucose positron emission tomography (}^{18}\text{FDG-PET)}$ scans, blood glucose was to be <160 mg/dl. $^{18}\text{FDG-PET}$ image evaluation was conducted centrally. Population pharmacodynamic models were used to link pharmacodynamic data to plasma copanlisib concentrations.
response assessments

A central review of the efficacy assessment for patients with non-Hodgkin’s lymphoma was performed retrospectively.

management and grading of hyperglycemia

Insulin administration at home was based on measurements of capillary blood glucose. CTCAE version 3.0 severity grading was applied to post-prandial blood glucose values following copanlisib infusion.

biomarker assessments

All biomarker analyses were retrospective and exploratory except for the requirement to enroll at least eight patients harboring \textit{PIK3CA} mutations in the solid-tumor expansion cohort. Tumor tissues (where available) and/or circulating tumor DNA from plasma collected at baseline were centrally assayed at screening for the presence of \textit{PIK3CA} mutations using beads, emulsions, amplification, and magnetics technology (Sysmex Inostics GmbH, Hamburg, Germany) in all cohorts. Additional assessments included: \textit{BRAF} and \textit{KRAS} mutational status in tumor and/or circulating tumor DNA (all cohorts); PTEN protein expression by immunohistochemistry of tumor samples (expansion cohorts only); and mutation analysis of a cancer gene panel (including PTEN) through next-generation sequencing of tumor samples (expansion cohorts only, when sufficient tumor material was available). PTEN immunohistochemical staining was evaluated based on staining intensity and percentage of stained cells.
Statistical analysis

This study was primarily a descriptive safety and tolerability trial and thus had no formal estimation of sample size. Summary statistics are used for all baseline characteristics and safety data. Frequency tables are provided for qualitative data. Efficacy analyses included descriptive analyses on response assessments by cohort, and within various biomarker-defined subgroups, as well as pharmacodynamic analyses of plasma glucose and insulin data. Fisher’s exact test was used to analyze the association between tumor response and biomarker findings.

Supplementary data

Safety

Elevated laboratory aspartate aminotransferase values were observed in 59% of patients (33/56) and were principally grade 1; grade ≥3 was observed in four patients. Laboratory alanine aminotransferase values were elevated in 34% of patients (19/56); all were grade 1, except for one patient in the 1.2 mg/kg cohort, with a grade 3 event and multiple other DLTs.

The two cases of drug-related grade 3 non-infectious pneumonitis occurred in cycles 3 and 16 and resolved within ~2 weeks with oral corticosteroids and interruption of study drug. The single case of grade 3 viral pneumonitis occurred in cycle 3 (CTCAE term “infection, bronchus”) and was not considered drug-related. All cases of pneumonitis occurred in patients with follicular lymphoma.
pharmacodynamics

Fifty-two patients (91%), including all patients treated at the MTD (0.8 mg/kg), had increases in plasma insulin more than twice baseline levels following copanlisib infusion, although use of short-acting insulin in a majority of patients confounded the interpretation of these results.

response

In the diffuse large B-cell lymphoma patient with a partial response, objective response could not be confirmed because of treatment discontinuation at cycle 10 as a result of a perirectal abscess. The two patients with diffuse large B-cell lymphoma who had disease progression discontinued from the study at the end of cycles 1 and 2, respectively.
### Table S1. Summary of treatment-emergent adverse events, regardless of causality

|                     | Dose-escalation cohorts | Expansion cohorts |        |
|---------------------|-------------------------|-------------------|--------|
|                     | Cohort 1 0.1 mg/kg     | Cohort 2 0.2 mg/kg| Cohort 3 0.4 mg/kg| Cohort 4 0.8 mg/kg| Cohort 5 1.2 mg/kg| Solid tumors 0.8 mg/kg| NHL 0.8 mg/kg| Diabetic 0.4 mg/kg| Total n (%) |
|                     | (n = 1)                 | (n = 3)           | (n = 3)          | (n = 7)           | (n = 3)           | (n = 25)           | (n = 9)     | (n = 6)           | (n = 57)    |
| Any AE, regardless  |                         |                   |                   |                   |                   |                   |             |                  |             |
| of causality<sup>a</sup> | 1 (100)                | 3 (100)          | 3 (100)          | 7 (100)          | 3 (100)          | 25 (100)          | 9 (100)     | 6 (100)          | 57 (100)    |
| AEs of grade 3 or 4, |                         |                   |                   |                   |                   |                   |             |                  |             |
| regardless of       |                         |                   |                   |                   |                   |                   |             |                  |             |
| causality           |                         |                   |                   |                   |                   |                   |             |                  |             |
| Grade 3             | 1 (100)                 | 3 (100)          | 3 (100)          | 5 (71)           | 2 (67)           | 17 (68)           | 7 (78)      | 3 (50)           | 41 (72)     |
| Grade 4             | 0                       | 0                 | 0                | 0                | 0                | 0                 | 1 (11)      | 0                | 1 (2)<sup>b</sup> |
| Grade 3 or 4 AEs in |                         |                   |                   |                   |                   |                   |             |                  |             |
| ≥5% of patients     |                         |                   |                   |                   |                   |                   |             |                  |             |
| regardless of       |                         |                   |                   |                   |                   |                   |             |                  |             |
| causality           |                         |                   |                   |                   |                   |                   |             |                  |             |
| Hyperglycemia       |                         |                   |                   |                   |                   |                   |             |                  |             |
| Grade 3             | 0                       | 0                 | 0                | 4 (57)           | 1 (33)           | 9 (36)           | 3 (33)      | 1 (17)           | 18 (32)     |
| Grade 4             | 0                       | 0                 | 0                | 1 (33)           | 0                | 0                | 0           | 0                | 1 (2)       |
| Hypertension        |                         |                   |                   |                   |                   |                   |             |                  |             |
| Grade 3             | 0                       | 0                 | 1 (33)           | 0                | 1 (33)           | 4 (16)           | 3 (33)      | 2 (33)           | 11 (19)     |
| Condition                        | Grade 3 | 0   | 3 (100) | 0   | 0   | 0   | 1 (4) | 1 (11) | 0   | 5 (9) |
|---------------------------------|---------|-----|---------|-----|-----|-----|-------|-------|-----|-------|
| Decreased hemoglobin            |         |     |         |     |     |     |       |       |     |       |
| Rash/desquamation               |         |     |         |     |     |     |       |       |     |       |
| Grade 3                         | 0       | 0   | 0       | 0   | 0   | 0   | 2 (8) | 1 (11) | 1 (17)| 4 (7) |

*a* All AEs were defined according to National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0.

*b* Two additional patients experienced a total of three grade 4 events, in addition to a grade 5 event each; therefore, the worst grade AE, regardless of causality, for these two patients was grade 5 and so they are not included here.

AE, adverse event; NHL, non-Hodgkin's lymphoma.
Table S2. Summary of grade 5 adverse events

| n (%) | Dose-escalation cohorts | Expansion cohorts |
|-------|-------------------------|-------------------|
|       | Cohort 1 0.1 mg/kg (n = 1) | Cohort 2 0.2 mg/kg (n = 3) | Cohort 3 0.4 mg/kg (n = 3) | Cohort 4 0.8 mg/kg (n = 7) | Cohort 5 1.2 mg/kg (n = 3) | Solid tumors 0.8 mg/kg (n = 25) | NHL 0.8 mg/kg (n = 9) | Diabetic 0.4 mg/kg (n = 6) | Total (n = 57) |
| Any grade 5 event, regardless of causality, n (%) | 0 | 0 | 0 | 1 (14) | 1 (33) | 4 (16) | 0 | 1 (17) | 7 (12) |
| Disease progression | 0 | 0 | 0 | 1 (14) | 0 | 2 (8) | 0 | 0 | 3 (5) |
| Colonic obstruction | 0 | 0 | 0 | 0 | 0 | 1 (4) | 0 | 0 | 1 (2) |
| Acute cardiac event\(^a\) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (17) | 1 (2) |
| Pericardial effusion\(^b\) | 0 | 0 | 0 | 0 | 1 (33) | 0 | 0 | 0 | 1 (2) |
| Vascular embolism\(^c\) | 0 | 0 | 0 | 0 | 0 | 1 (4) | 0 | 0 | 1 (2) |

\(^a\)Either pulmonary embolism or myocardial infarction.

\(^b\)Pericardial effusion developed within 2 weeks of grade 3 left ventricular systolic dysfunction (dose-limiting toxicity) and was associated with progressive disease.
Patnaik et al. Annals of Oncology 2016

*Adverse event associated with progressive disease.

NHL, non-Hodgkin’s lymphoma.
**Table S3.** Mean HbA1c levels at baseline and following treatment with copanlisib

|                          | Non-diabetic patients (n = 36) | Raised baseline HbA1c (HbA1c 5.7–6.5%) (n = 12) | Diabetic patients (HbA1c >6.5%) (n = 7) |
|--------------------------|-------------------------------|-----------------------------------------------|------------------------------------------|
| HbA1c, %, mean ± SEM     |                               |                                               |                                          |
| At baseline              | 5.4 ± 0.3                     | 6.0 ± 0.2                                     | 7.4 ± 1.2                                |
| After treatment with copanlisib | 5.9 ± 0.5                    | 6.3 ± 0.7                                     | 7.3 ± 1.1                                |

*Diabetic patients received short-acting insulin and oral glucose-lowering agents following copanlisib infusion.

HbA1c, hemoglobin A1c; SEM, standard error of the mean.
**Table S4.** Systolic blood pressure at baseline and following treatment with copanlisib: patients in the MTD expansion cohort

|                      | Solid-tumor expansion cohort 0.8 mg/kg (n = 25) |
|----------------------|-----------------------------------------------|
|                      | Day 1  | Day 2  | Day 8  |
| Systolic blood pressure, mmHg, mean ± SD |                      |        |        |
| Pre-infusion         | 118.4 ± 13.6 | -      | 119.4 ± 11.3 |
| 1.5 h post-infusion with copanlisib | 143.6 ± 18.3 | -      | -      |
| 25 h post-start of infusion with copanlisib | -      | 121.2 ± 15.7 | -      |

MTD, maximum tolerated dose; SD, standard deviation.
### Table S5. Mutation analysis of *PIK3CA* and *KRAS*

| Patient ID | Tumor type            | Best response | PIK3CA assay | PIK3CA mutation status | PIK3CA mutation<sup>a</sup> | KRAS assay | KRAS mutation status | KRAS mutation<sup>a</sup> |
|------------|------------------------|---------------|--------------|------------------------|----------------------------|------------|---------------------|---------------------------|
|            |                        |               |              |                        |                            |            |                     |                           |
| **Cohort 1 (0.1 mg/kg)** |                        |               |              |                        |                            |            |                     |                           |
| 140022001  | Esophageal             | SD            | P            | WT                     | -                          | P          | WT                  | -                         |
| **Cohort 2 (0.2 mg/kg)** |                        |               |              |                        |                            |            |                     |                           |
| 140011001  | Ewing’s sarcoma        | PD            | P            | WT                     | -                          | P          | WT                  | -                         |
| 140022002  | Rectal melanoma        | PD            | P            | WT                     | -                          | P          | WT                  | -                         |
| 140022003  | Gastric liposarcoma    | SD            | P            | WT                     | -                          | P          | WT                  | -                         |
| **Cohort 3 (0.4 mg/kg)** |                        |               |              |                        |                            |            |                     |                           |
| 140011002  | Bladder                | PD            | P            | WT                     | -                          | P          | WT                  | -                         |
| 140022004  | Uterine                | SD            | P            | WT                     | -                          | P          | mut g35a/G12D       |                           |
| 140022005  | Pelvic leiomyosarcoma   | SD            | P/T          | WT                     | -                          | P/T        | WT                  | -                         |
| **Cohort 4 (0.8 mg/kg)** |                        |               |              |                        |                            |            |                     |                           |
| 140011003  | NSCLC                  | PD            | P            | WT                     | -                          | P          | WT                  | -                         |
| 140011005  | Pancreatic             | NA            | P            | WT                     | -                          | P          | mut g35a/G12D       |                           |
| 140011006  | Cholangiocarcinoma     | SD            | P            | WT                     | -                          | P          | WT                  | -                         |
| Cohort          | Tumor Type                          | Status | PD/P/T/N | Mutation                      | WT/WT/WT | P/T/WT | - | - |
|----------------|-------------------------------------|--------|----------|-------------------------------|----------|--------|---|---|
| 140011007      | Pancreatic                          | PD     | P        | WT                            | P        | mut   | g34c/G12R |
| 140022008      | Endometrial                         | PD     | P/T      | mut<sup>b</sup> a3140g (OOS)/H1047R | P/T      | WT    | - |
| 140022009      | Medullary thyroid                    | SD     | P/T      | WT                            | P/T      | WT    | - |
| 140022010      | Esophageal                          | PD     | P/T      | WT                            | P/T      | WT    | - |
| Cohort 5 (1.2 mg/kg) |                                |        |          |                               |          |        |   |   |
| 140011008      | Colon                               | NA     | P        | WT                            | P        | WT    | - |
| 140022011      | Peritoneal neuroendocrine           | SD     | P/T      | WT                            | P/T      | WT    | - |
| 140033002      | Pancreatic                          | NA     | P        | WT                            | P        | WT    | - |
| Solid-tumor expansion cohort (0.8 mg/kg) |                         |        |          |                               |          |        |   |   |
| 140011101      | Bladder                             | PD     | P/T/N    | mut<sup>c</sup> a1637g/Q546R  | N        | WT    | - |
| 140022103      | Bladder                             | SD     | P/T      | WT                            | -        | -     | - |
| 140022104      | Breast (ER+ PR+ HER2/neu−)          | SD     | P/T      | mut<sup>d</sup> a3140t/H1047L | P        | WT    | - |
| 140022105      | Breast (ER+ PR+ HER2/neu−)          | PRc    | P        | WT                            | P        | WT    | - |
| 140022108      | Gastric                             | NA     | P/T/N    | WT                            | N        | mut   | g35t/G12V |
| 140022111      | Breast (TNBC)                       | PD     | P/T      | WT                            | P        | WT    | - |
| 140022112      | Breast (TNBC)                       | SD     | P/T      | WT                            | P        | WT    | - |
| Sample ID  | Tissue Type    | PD/SD/CR | T/P/N | Mutation 1 | Mutation 2 | Mutation 3 | Mutation 4 | Mutation 5 | Status |
|----------------|----------------|----------|-------|------------|------------|------------|------------|------------|--------|
| 140022113     | Breast (ER+ PR+ HER2/neu−) | PD | P/T | mut | a3140g/H1047R | P | WT | - |
| 140022114     | Breast (ER+ PR+ HER2/neu−) | PD | P/T | mut | a3140g/H1047R | P | WT | - |
| 140022115     | Breast (TNBC)   | PD | P/T | WT | - | P | WT | - |
| 140022116     | Endometrial     | SD | P/T | WT | - | P | WT | - |
| 140022117     | Endometrial     | SD | P/T | WT | - | P | WT | - |
| 140022119     | Breast (TNBC)   | NA | P/T/N | WT | - | N | WT | - |
| 140022120     | Breast (ER+ PR+ HER2/neu−) | PD | P/T | mut | a3140g/H1047R | P | WT | - |
| 140022121     | Breast (ER+ PR+ HER2/neu+) | PD | P/T | mut | g1624a/E542K, g1633a/E545K | P | WT | - |
| 140022129     | Ovarian         | PD | P/T/N | WT | - | N | WT | - |
| 140033102     | Breast (ER+ PR+ HER2/neu+) | PRu | P/T/N | mut | g1638t/Q546H | N | WT | - |
| 140033103     | Ovarian         | PD | P/T/N | WT | - | N | WT | - |
| 140033104     | Gastric         | PD | P/T | WT | - | - | - | - |
| 140033105     | Breast (ER+ PR+ HER2/neu unknown) | SD | P/T/N | mut | a3140g/H1047R | N | mut | g535a/G179S |
| 140033106     | Endometrial     | CR | P/T/N | mut | c3155a/T1052K, g263t/R88L, 1359_1361delAGA/E453del | N | WT | - |
| Subheading                                                                 | Case     | Stage | Response | Status | Mutation       | Response | Status | Mutation       |
|---------------------------------------------------------------------------|----------|-------|----------|--------|----------------|----------|--------|----------------|
| **Diabetic expansion cohort (0.4 mg/kg)**                                 |          |       |          |        |                |          |        |                |
| 140011104 Gastric                                                         | PD       | P/T/N | mut      | g1624a/E542K | N             | mut     | g35a/G12D |
| 140011105 NSCLC                                                           | NA       | P/N   | WT       | -      | N             | mut     | g34t/G12C |
| 140011106 Colon                                                           | PD       | P/T/N | WT       | -      | N             | WT      | -       |
| 140011107 Bladder                                                         | PD       | P     | WT       | -      | P             | WT      | -       |
| 140011109 NSCLC                                                           | PD       | P     | WT       | -      | P             | mut     | a183c/Q61H |
| 140011110 Ovarian                                                         | PD       | P/T/N | WT       | -      | N             | WT      | -       |
| **NHL expansion cohort (0.8 mg/kg)**                                      |          |       |          |        |                |          |        |                |
| 140022101 Follicular lymphoma                                             | CR       | P/T   | WT       | -      | -             | -        | -      |
| 140022106 Follicular lymphoma                                             | PR       | P/T   | WT       | -      | P             | WT      | -       |
| 140022110 Follicular lymphoma                                             | PR       | P     | WT       | -      | P             | WT      | -       |
| 140022122 Follicular lymphoma                                             | PR       | P/T/N | WT       | -      | N             | WT      | -       |
### Table of Results

| Sample ID   | Tumor Type          | Status | T/P | WT   | Mut Status | Amino Acid Change |
|-------------|---------------------|--------|-----|------|------------|------------------|
| 140022126   | Follicular lymphoma | PR     | P/T | WT   | -          | -                |
| 140022128   | DLBCL               | PD     | P/T | WT   | -          | -                |
| 140022130   | Follicular lymphoma | CR     | P   | WT   | -          | P WT             |
| 140022131   | DLBCL               | PR     | P/T | WT   | -          | -                |
| 140033114   | DLBCL               | PD     | P/N | WT   | -          | N WT             |

*a*Mutation includes nucleotide change/amino acid change.

*b*Mutation was detected by tumor BEAMing only (sample was wild type by plasma BEAMing, and the mutation detected in tumor tissue was out of specification but detectable).

*c*Mutation was detected by tumor next-generation sequencing only (sample was wild type by tumor BEAMing and plasma BEAMing, although the specific mutations detected by next-generation sequencing were not tested for using the directed BEAMing mutation assay).

*d*Mutation was detected by BEAMing of plasma only (sample was wild type by tumor BEAMing).

BEAMing, beads, emulsions, amplification, and magnetics technology; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ER/PR, estrogen receptor/progesterone receptor; HER2, human epidermal growth factor receptor 2; mut, mutation; N, mutational status was assessed using next-generation sequencing of DNA isolated from tumor tissue; NA, not available; NSCLC, non-small-cell lung cancer; P, mutational status was assessed from DNA isolated from plasma sample by BEAMing (Sysmex Inostics GmbH, Hamburg, Germany); PD, progressive disease; PR, partial response; PRc, confirmed partial response; PRu, unconfirmed partial response; SD, stable disease; T, mutational status was assessed from DNA isolated from tumor by BEAMing; TNBC, triple-negative breast cancer; WT, wild type.
**Figure S1.** Measurement of blood glucose (A) and systolic blood pressure (B) for patients ($n = 25$) from the 0.8 mg/kg dose cohort during the first treatment cycle. Values were measured from the start of the 1-h infusion. Fasting was required 8 h before the infusion and 2 h after the end of the infusion. Samples were collected at 0 h on day 8.

A

B
**Figure S2.** Plasma glucose maximum change from baseline versus copanlisib $\text{AUC}_{(0-25)}$. 

$\text{AUC}_{(0-25)}$, area under the curve from time zero to 25 h after start of infusion.
Figure S3. Percentage change from baseline in SUV_{max} from $^{18}$FDG-PET versus exposure of copanlisib. $^{18}$FDG-PET, $[^{18}F]$-fluorodeoxyglucose positron emission tomography; AUC_{(0–25)}, area under the curve from time zero to 25 h after start of infusion; SUV_{max}, maximum standardized uptake.