Sponsor

Novartis

Generic Drug Name

AUY922

Therapeutic Area of Trial

Advanced solid malignancies

Approved Indication

Investigational

Protocol Number

CAUY922A1101

Title

A Japanese phase I, multi-center, open-label, study of AUY922 administered intravenously on a once weekly schedule in adult patients with advanced solid malignancies

Study Phase

Phase I

Study Start/End Dates

11 Nov 2008 to 07 May 2012

Study Design/Methodology

This was a phase I, multi-center, open-label, dose-escalation trial in which AUY922 was to be administered intravenously on a once-weekly schedule. An adaptive Bayesian logistic regression model (BLRM) guided by the escalation with overdose control (EWOC) principle guided the dose escalation of treatment with AUY922 to determine the MTD. The starting dose for this study was 8 mg/m2. Decisions regarding subsequent dose levels were made based on discussions between investigators and the sponsor at the dose escalation meetings. The determination of the MTD was based on the incidence of dose-limiting toxicities (DLTs) during Cycle 1. In principle, a cycle was 28 days.

Centers

Two centers in Japan.

Publication

None

Test Product (s), Dose(s), and Mode(s) of Administration

AUY922 was supplied in individual 10 mL amber-colored glass ampoules, each containing 10 mL of a 5 mg/mL active drug substance in 5% aqueous glucose solution. AUY922 was diluted to the appropriate concentration (according to the patient's body surface area [BSA]) in a 500 mL infusion bag containing 5% dextrose or glucose (with a maximum infusion volume of 500 mL) prior to administration. AUY922 was administered intravenously over 1 hour.

Statistical Methods

All statistical procedures were performed with WinBUGS or SAS Version 9.2. PK parameters were calculated using non compartmental techniques with WinNonlin Version 5.2.

Analysis sets

The FAS included all patients who had received at least one dose of AUY922. Patients were classified according to the intended treatment. Patients who were screened but never started treatment were listed. Screening failures were not included in any of the summary tables.

The safety set included all patients who had received at least one dose of AUY922 and had at least one valid post-baseline safety assessment. The statement that a patient had no AEs (on the Adverse Event eCRF) constituted a valid safety assessment. Patients were classified according to treatment received, where treatment received was defined as (i) the treatment assigned if it was received at least once, or (ii) the first treatment received when starting therapy with study medication. Each patient was classified into and analyzed consistently within one (and only one) treatment group.

Per-protocol set (PPS)

The PPS consisted of all patients in the FAS who were compliant with the protocol in the following ways:

1. The diagnosis corresponded to that defined in the inclusion criteria.
2. The stage of disease corresponded to that defined in the inclusion criteria.
3. Prior treatment corresponded to that defined in the inclusion criteria.
4. The patient was evaluated at least once for the primary efficacy variable, discontinued due to AE or disease progression, or died prior to the first evaluation of the primary efficacy variable.
5. No other major protocol violations had occurred.

Patients were classified according to the intended treatment.

Dose-determining set

The dose-determining set consisted of all patients from the safety set who either met the following minimum exposure criteria and had sufficient safety evaluations, or discontinued earlier but experienced a DLT (refer to Section 9.4.6.4.9). The minimum exposure criteria were that a patient had to a) have been treated with AUY922 for at least 3 doses in Cycle 1,

b) have been observed for ≥ 28 days following the first dose, and c) have completed all required safety evaluations, or have experienced a DLT. This constituted an evaluable patient for the determination of the MTD. Patients who did not meet these minimum safety evaluation requirements were regarded as ineligible for inclusion into the dose-determining set. Patients in the dose-determining set were identified prior to the DBL. In some tables and listings of this report, the term "MTD determining analysis set", which means the same as "dose-determining set", is also used.

Patients were classified according to the intended treatment.

In unexpected situations where patients had an incorrect dose throughout Cycle 1, an actual dose given was to be used.

PK set

The PK set consisted of all FAS patients who had at least one available PK measurement. The analysis set was used for PK concentration summaries, PK parameter summaries, and PK analysis. Patients were classified according to the intended treatment.

The data at the time of the data cut-off date of 5 July 2011 are used in the tables, figures, and listings generated from the statistical analysis using the PK set and dose-determining set. All planned data for these analyses sets had been collected by 5 July 2011. For the other tables, figures, and listings in this report, the data at the time of database lock (20 June 2012) was used.

Primary efficacy end point

The primary objective of this study was the determination of the MTD of AUY922

The MTD was defined to be the highest dose of AUY922 given for at least 3 doses in the first treatment cycle in which it was expected to produce medically unacceptable dose-limiting toxicities in < 33% of patients. The criteria of MTD was the actual administered dose with the highest posterior probability of DLTs in the target interval [16%, 33%) among the doses fulfilling the overdose criteria. In this study, at least 15 patients were to be enrolled for the model to have reasonable operating characteristics relating to its MTD recommendation and at least 6 patients were to be enrolled at the MTD level.

Secondary efficacy end point

Overall response rate (CR or PR), disease control (CR, PR, or stable disease) and best overall response were evaluated using the FAS.

Best overall response, overall response rate, and disease control rate were summarized.

Overall response rate and disease control rate were summarized with 95% confidence interval (CI). The assessment of safety was based on the type, severity, and frequency of AEs and on the number of laboratory values that fell outside of the pre-determined ranges. The baseline observation was to be the last observation at baseline. All safety data were listed. The safety set was used for summary.

The primary analysis method used was an adaptive BLRM guided by the EWOC principle. All information currently available about the dose-toxicity curve of AUY922 was summarized in a prior distribution. For this study, available data included pre-clinical data for

AUY922 and clinical data from the Western first-in-human study in patients with advanced solid malignancies (CAUY922A2101). This prior distribution was then updated after each cohort of patients with the DLT data from the current trial.

Descriptive statistics of PK parameters included arithmetic mean, geometric mean, standard deviation (SD), median, minimum, maximum, coefficient of variation (CV) (%) for arithmetic mean, and CV (%) for geometric mean. The relationship between dose and PK parameters (Cmax, AUClast, and AUCinf) of AUY922 and BJP762 was explored based on the power model, $\ln(PK) = a+\beta\ln(dose)+error$.

No formal interim analyses were planned or performed.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria

Patients were eligible for enrollment in the study if they met all of the following inclusion criteria:

1. Patients with histologically confirmed, advanced solid malignancies (surgically unresectable locally advanced and/or metastatic solid malignancies) whose disease had progressed on at least one line of standard systemic therapy or for whom no standard therapy existed.
2. At least one measurable or non-measurable lesion as defined by Response Evaluation Criteria in Solid Tumors (RECIST).
3. Age ≥ 20 years.
4. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of ≤ 2.
5. Life expectancy of ≥ 12 weeks.
6. The following laboratory values:
   - Absolute neutrophil count (ANC) ≥ 1.5×10^9/L
   - Hemoglobin (Hgb) ≥ 8.5 g/dL
   - PLT ≥ 100×10^9/L
   - Potassium within normal institutional limits or correctable with supplements
   - Total calcium (corrected for serum albumin) within institutional normal limits or correctable with supplements
   - Magnesium within institutional normal limits or correctable with supplements
   - Phosphorus within institutional normal limits or correctable with supplements
   - Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase [SGOT]) and alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase [SGPT]) ≤ 2.5 × upper limit of normal (ULN)
   - Serum bilirubin ≤ 1.5 × ULN
   - Serum albumin ≥ 2.5 g/dL
   - Serum creatinine ≤ 1.5 × ULN or 24-hour clearance ≥ 50 mL/min
   - Negative serum pregnancy test: the serum pregnancy test had to have been conducted prior to the first administration of AUY922 (≤ 7 days prior to dosing) in all premenopausal women and women < 2 years after the onset of menopause.

7. Ability to sign the informed consent form and to comply with the protocol.
8. Willingness and ability to consent to hospitalization for the duration of the first treatment cycle.

Exclusion criteria

Patients were excluded from enrollment in the study if they met any of the following exclusion criteria:

1. Known central nervous system (CNS) metastasis or primary CNS tumors. Patients without clinical signs or symptoms of CNS involvement were not required to have a computerized tomography (CT) or magnetic resonance imaging (MRI) of the brain.
2. Prior treatment with any HSP90 or histone deacetylase inhibitor compound.
3. Receipt of systemic anticancer treatment prior to the first dose of AUY922 within the following time frames:
   - Radiotherapy within 4 weeks
   - Palliative radiotherapy within 2 weeks
   - Nitrosoureas, mitomycin, and monoclonal antibodies, such as trastuzumab within 6 weeks
   - Conventional chemotherapy, hormonal therapy, and immunotherapy within 4 weeks
   - Any continuous dosing (i.e. daily dosing, every-other-day dosing, Monday-Wednesday-Friday dosing, weekly dosing, etc.) of systemic anticancer treatment for which the recovery period was not known, or investigational drugs (i.e. targeted agents) within a duration of ≤ 5 half-lives of the agent and their active metabolites (if any)
   - Major surgery within 4 weeks
4. Lack of recovery from side effects of previous systemic anticancer therapy to ≤ National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) grade 1 prior to the first dose of study treatment (except for alopecia).
5. Other concurrent severe and/or uncontrolled medical conditions (e.g. uncontrolled diabetes and active or uncontrolled infection) that could cause unacceptable safety risks or compromise compliance with the protocol.
6. Patients with clinically significant heart disease.
7. Known disorders due to a deficiency in bilirubin glucuronidation (e.g. Gilbert's syndrome).

Participant Flow

Patient disposition, by treatment (FAS)

	AUY922 8 mg/m^2 N=3 n (%)	AUY922 16 mg/m^2 N=3 n (%)	AUY922 22 mg/m^2 N=3 n (%)	AUY922 28 mg/m^2 N=5 n (%)	AUY922 40 mg/m^2 N=3 n (%)	AUY922 54 mg/m^2 N=6 n (%)	AUY922 70 mg/m^2 N=8 n (%)	All patients N=31 n (%)
Patients treated								

Treatment ended	3 (100.0)	3 (100.0)	3 (100.0)	5 (100.0)	3 (100.0)	6 (100.0)	8 (100.0)	31 (100.0)
Primary reason for end of treatment								
AEs	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (12.5)	2 (6.5)
Disease progression	3 (100.0)	3 (100.0)	3 (100.0)	5 (100.0)	3 (100.0)	5 (83.3)	7 (87.5)	29 (93.5)

Baseline Characteristics

Demographics and baseline characteristics, by treatment (FAS)

Demographic variables	AUY922 8 mg/m^2 N=3	AUY922 16 mg/m^2 N=3	AUY922 22 mg/m^2 N=3	AUY922 28 mg/m^2 N=5	AUY922 40 mg/m^2 N=3	AUY922 54 mg/m^2 N=6	AUY922 70 mg/m^2 N=8	AUY922 All Patients N=31
Age (years)								
n	3	3	3	5	3	6	8	31
Mean	51.3	61.7	52.7	53.6	62.0	62.3	59.4	58.1
SD	17.95	2.08	1.15	6.35	9.00	6.02	11.49	9.34
Median	58.0	61.0	52.0	54.0	62.0	64.5	62.5	60.0
Minimum	31.0	60.0	52.0	45.0	53.0	54.0	36.0	31.0
Maximum	65.0	64.0	54.0	61.0	71.0	69.0	71.0	71.0
Age group (years)								
<65	2(66.7%)	3(100%)	3(100%)	5(100%)	2(66.7%)	3(50.0%)	6(75.0%)	24(77.4%)
≥65	1(33.3%)	0(0.0%)	0(0.0%)	0(0.0%)	1(33.3%)	3(50.0%)	2(25.0%)	7(22.6%)
Sex								
Male	2(66.7%)	1(33.3%)	3(100%)	2(40.0%)	1(33.3%)	2(33.3%)	4(50.0%)	15(48.4%)
Female	1(33.3%)	2(66.7%)	0(0.0%)	3(60.0%)	2(66.7%)	4(66.7%)	4(50.0%)	16(51.6%)
Race								
Asian	3(100%)	3(100%)	3(100%)	5(100%)	3(100%)	6(100%)	8(100%)	31(100%)
Height (cm)								
n	3	3	3	5	3	6	8	31
Mean	166.7	157.7	167.3	160.0	154.0	159.3	158.5	160.0
SD	9.50	10.79	1.53	10.77	5.29	5.32	8.43	8.20
Median	167.0	153.0	167.0	163.0	152.0	159.5	158.5	160.0
Minimum	157.0	150.0	166.0	145.0	150.0	153.0	147.0	145.0
Maximum	176.0	170.0	169.0	174.0	160.0	168.0	173.0	176.0
Weight (kg)								
n	3	3	3	5	3	6	8	31
Mean	61.0	53.5	56.8	52.6	56.9	57.0	52.5	55.2

SD	14.20	10.95	5.81	14.06	7.62	5.59	7.01	8.86
Median	65.3	48.1	56.5	53.3	52.5	55.6	53.0	53.3
Minimum	45.1	46.3	51.2	33.3	52.5	51.9	38.1	33.3
Maximum	72.5	66.1	62.8	70.2	65.7	67.1	61.0	72.5
Weight group (kg)								
<55	1(33.3%)	2(66.7%)	1(33.3%)	3(60.0%)	2(66.7%)	3(50.0%)	6(75.0%)	18(58.1%)
55-<75	2(66.7%)	1(33.3%)	2(66.7%)	2(40.0%)	1(33.3%)	3(50.0%)	2(25.0%)	13(41.9%)
BSA (m^2)								
n	3	3	3	5	3	6	8	31
Mean	1.7	1.5	1.6	1.5	1.5	1.6	1.5	1.6
SD	0.23	0.21	0.07	0.24	0.13	0.08	0.14	0.15
Median	1.8	1.4	1.6	1.6	1.5	1.6	1.5	1.5
Minimum	1.4	1.4	1.6	1.2	1.5	1.5	1.3	1.2
Maximum	1.8	1.8	1.7	1.8	1.7	1.7	1.7	1.8
LVEF (%) at baseline								
n	3	3	3	5	3	6	8	31
Mean	68.0	64.3	64.7	66.9	67.8	63.9	67.1	66.1
SD	7.00	2.89	4.51	7.12	6.25	5.05	5.90	5.43
Median	68.0	66.0	65.0	67.0	66.9	64.0	66.5	66.0
Minimum	61.0	61.0	60.0	58.7	62.0	56.2	61.1	56.2
Maximum	75.0	66.0	69.0	77.0	74.4	69.0	80.0	80.0
ECOG PS								
0	2(66.7%)	3(100%)	2(66.7%)	3(60.0%)	3(100%)	4(66.7%)	4(50.0%)	21(67.7%)
1	1(33.3%)	0(0.0%)	1(33.3%)	2(40.0%)	0(0.0%)	2(33.3%)	4(50.0%)	10(32.3%)

Outcome measures

Primary Outcome Result(s)

DLTs during Cycle 1 by treatment (dose-determining set)

	AUY922 8 mg/m^2 N=3 n (%)	AUY922 16 mg/m^2 N=3 n (%)	AUY922 22 mg/m^2 N=3 n (%)	AUY922 28 mg/m^2 N=4 n (%)	AUY922 40 mg/m^2 N=3 n (%)	AUY922 54 mg/m^2 N=6 n (%)	AUY922 70 mg/m^2 N=6 n (%)	All patients N=28 n (%)
-Total	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (3.6)

Summary of posterior distribution of DLT (dose-determining set)

Dose (mg/m^2)	Interval probabilities			Mean	SD	Quantiles		
	0-0.16	0.16-0.33	0.33-1			2.5%	50%	97.5%
70	0.655	0.313	0.032	0.142	0.083	0.029	0.126	0.344
75	0.596	0.351	0.052	0.156	0.092	0.031	0.138	0.383
80	0.545	0.377	0.078	0.170	0.102	0.033	0.149	0.422
85	0.499	0.394	0.107	0.183	0.112	0.035	0.160	0.462
90	0.459	0.403	0.138	0.197	0.121	0.037	0.171	0.502
95	0.424	0.408	0.168	0.211	0.131	0.039	0.182	0.540
100	0.393	0.407	0.199	0.224	0.140	0.041	0.193	0.576
105	0.366	0.406	0.227	0.237	0.149	0.042	0.204	0.610
110	0.344	0.401	0.255	0.249	0.157	0.044	0.214	0.643
Recommended dose for Phase II study						70 mg/m^2		

Secondary Outcome Result(s)

Best overall response (FAS)

	AUY922 8 mg/m^2 N=3	AUY922 16 mg/m^2 N=3	AUY922 22 mg/m^2 N=3	AUY922 28 mg/m^2 N=5	AUY922 40 mg/m^2 N=3	AUY922 54 mg/m^2 N=6	AUY922 70 mg/m^2 N=8	All patients N=31
Best overall response								
Complete response	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Partial response	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	1 (3.2%)
Stable disease	1 (33.3%)	1 (33.3%)	0 (0.0%)	1 (20.0%)	1 (33.3%)	1 (16.7%)	5 (62.5%)	10 (32.3%)
Progressive disease	2 (66.7%)	2 (66.7%)	3 (100%)	4 (80.0%)	2 (66.7%)	3 (50.0%)	3 (37.5%)	19 (61.3%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	1 (3.2%)
Not assessed	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Summary of blood AUY922 PK parameters (PK set)

PK Parameter	AUY922 8mg/m^2 N=3	AUY922 16mg/m^2 N=3	AUY922 22mg/m^2 N=3	AUY922 28mg/m^2 N=5	AUY922 40mg/m^2 N=3	AUY922 54mg/m^2 N=6	AUY922 70mg/m^2 N=8

Profile Day :Cycle 1 Day 1							
Tmax (hr)							
n	3	3	3	5	3	6	8
Median	1.08	1.03	0.500	0.500	1.05	0.759	1.02
Minimum	0.500	0.483	0.500	0.483	0.500	0.483	0.233
Maximum	1.58	1.08	1.08	1.07	1.05	1.17	1.17
Cmax (ng/mL)							
n	3	3	3	5	3	6	8
Mean	168	329	429	457	710	1050	1100
SD	22.0	28.1	42.6	101	42.4	118	118
CV%	13.0	8.53	9.93	22.1	5.98	11.3	10.7
AUClast (hr·ng/mL)							
n	3	3	3	5	3	6	8
Mean	3520	4990	6510	6810	6960	8880	8540
SD	721	692	1850	1090	1270	1710	895
CV%	20.5	13.9	28.4	16.0	18.2	19.3	10.5
AUCinf (hr.ng/mL)							
n	3	3	3	5	2	5	8
Mean	4120	6370	9070	9550	11400	12300	12600
SD	1150	923	3210	2460	3470	2720	1720
CV%	28.0	14.5	35.4	25.8	30.5	22.1	13.7
CL (L/hr)							
n	3	3	3	5	2	5	8
Mean	3.38	3.91	4.29	4.79	5.74	7.24	8.60
SD	0.801	0.856	1.33	1.68	1.16	1.97	1.30
CV%	23.7	21.9	31.1	35.1	20.3	27.2	15.1
Vz (L)							
n	3	3	3	5	2	5	8
Mean	306	425	582	646	980	1190	1570
SD	40.5	80.9	120	111	132	151	293
CV%	13.2	19.0	20.5	17.1	13.4	12.7	18.6
T1/2 (hr)							
n	3	3	3	5	2	5	8
Mean	64.1	75.8	96.4	98.7	123	120	127
SD	10.5	4.10	11.9	23.0	40.8	28.5	18.8
CV%	16.4	5.42	12.3	23.3	33.3	23.7	14.7
Profile Day : Cycle 2 Day 1							
Tmax (hr)							
n	2	2	3	2	2	5	6
Median	0.767	0.775	0.500	0.767	0.500	1.05	0.500
Minimum	0.500	0.517	0.500	0.483	0.500	0.483	0.217
Maximum	1.03	1.03	1.07	1.05	0.500	1.17	1.05
Cmax (ng/mL)							
n	2	2	3	2	2	5	6

Mean	214	359	446	454	779	1050	1230
SD	2.12	8.49	37.3	5.66	38.2	81.6	234
CV%	0.994	2.36	8.35	1.25	4.90	7.75	19.0
AUClast (hr·ng/mL)							
n	2	2	2	2	2	5	6
Mean	6140	6040	7560	7180	7590	8800	9520
SD	3050	227	2040	280	268	1410	1120
CV%	49.6	3.76	27.0	3.90	3.53	16.0	11.7

Summary of blood BJP762 PK parameters (PK set)

PK Parameter	AUY922 8mg/m^2 N=3	AUY922 16mg/m^2 N=3	AUY922 22mg/m^2 N=3	AUY922 28mg/m^2 N=5	AUY922 40mg/m^2 N=3	AUY922 54mg/m^2 N=6	AUY922 70mg/m^2 N=8
Profile Day : Cycle 1 Day 1							
Tmax (hr)							
n	3	3	3	5	3	6	8
Median	1.08	1.08	1.17	1.07	1.05	1.08	1.13
Minimum	1.05	1.03	1.08	1.05	1.05	1.02	1.00
Maximum	1.13	1.17	1.18	1.17	1.07	1.22	1.23
Cmax (ng/mL)							
n	3	3	3	5	3	6	8
Mean	135	253	347	611	964	1060	1330
SD	51.5	2.89	192	201	775	569	904
CV%	38.3	1.14	55.4	32.9	80.5	53.7	67.8
AUClast (hr·ng/mL)							
n	3	3	3	5	3	6	8
Mean	732	1890	2520	3700	5690	6320	5530
SD	480	568	2030	2170	5250	4650	3320
CV%	65.6	30.1	80.8	58.6	92.2	73.6	60.0
AUCinf (hr·ng/mL)							
n	3	3	3	5	3	5	6
Mean	778	1950	2710	3940	5830	6770	5020
SD	491	559	1960	2320	5300	5200	3340
CV%	63.0	28.7	72.5	58.9	90.9	76.8	66.5
T1/2 (hr)							
n	3	3	3	5	3	5	6
Mean	31.8	33.5	67.9	59.1	33.1	49.1	46.5
SD	15.3	15.1	47.5	28.8	12.1	24.0	27.9
CV%	48.0	45.2	70.0	48.7	36.5	48.8	60.0
Profile Day : Cycle 2 Day 1							
Tmax (hr)							
n	2	2	3	2	2	5	6
Median	1.09	1.13	1.17	1.13	1.11	1.17	1.21
Minimum	1.03	1.03	1.07	1.05	1.10	1.13	1.02

Maximum	1.15	1.22	1.22	1.20	1.12	1.20	1.37
Cmax (ng/mL)							
n	2	2	3	2	2	5	6
Mean	99.9	234	550	439	603	1100	1340
SD	62.4	40.3	456	78.5	373	393	1260
CV%	62.4	17.3	83.0	17.9	61.9	35.8	94.1
AUClast (hr·ng/mL)							
n	2	2	2	2	2	5	6
Mean	454	1160	2020	2600	2840	5210	5310
SD	294	364	881	791	2180	2490	4130
CV%	64.8	31.3	43.7	30.4	76.8	47.8	77.7

Safety Results

AEs (CTCAE all grades and grade 3 or 4), regardless of study drug relationship, by primary SOC, and preferred term (safety set)

	AUY922 8 mg/m^2 N=3		AUY922 16 mg/m^2 N=3		AUY922 22 mg/m^2 N=3		AUY922 28 mg/m^2 N=5	
Primary SOC Preferred term	**All grades n (%)**	**Grade 3/4 n (%)**	**All grades n (%)**	**Grade 3/4 n (%)**	**All grades n (%)**	**Grade 3/4 n (%)**	**All grades n (%)**	**Grade 3/4 n (%)**
Any primary SOC								
-Total	3(100.0)	1(33.3)	3(100.0)	0(0.0)	3(100.0)	2(66.7)	5(100.0)	2(40.0)
Blood and lymphatic system disorders								
-Total	1(33.3)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	3(60.0)	0(0.0)
Anaemia	1(33.3)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Lymphopenia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)
Neutropenia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiac disorders								
-Total	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Atrioventricular block first degree	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Bradycardia	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Cardiac discomfort	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Sinus bradycardia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ventricular arrhythmia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Eye disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(66.7)	0(0.0)	3(60.0)	0(0.0)
Cataract	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Conjunctival haemorrhage	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Diplopia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Eye disorder	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Eye pruritus	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Eyelid oedema	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Glaucoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Night blindness	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(66.7)	0(0.0)	2(40.0)	0(0.0)
Photophobia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Photopsia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(20.0)	0(0.0)
Retinopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vision blurred	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)
Visual acuity reduced	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Visual impairment	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vitreous floaters	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Gastrointestinal disorders								
-Total	0(0.0)	0(0.0)	2(66.7)	0(0.0)	3(100.0)	0(0.0)	5(100.0)	1(20.0)
Abdominal pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Abdominal pain upper	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Anal inflammation	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Cheilitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Constipation	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Diarrhoea	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(66.7)	0(0.0)	4(80.0)	0(0.0)
Dyspepsia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Frequent bowel movements	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Ileus paralytic	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Mallory-Weiss syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nausea	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Oesophageal fistula	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	1(20.0)
Rectal haemorrhage	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Stomatitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vomiting	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
General disorders and administration site conditions								
-Total	1(33.3)	0(0.0)	2(66.7)	0(0.0)	1(33.3)	0(0.0)	3(60.0)	1(20.0)
Chest discomfort	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Fatigue	1(33.3)	0(0.0)	1(33.3)	0(0.0)	1(33.3)	0(0.0)	2(40.0)	0(0.0)
Influenza like illness	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Injection site pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Localised oedema	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Malaise	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Oedema peripheral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Pyrexia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	1(20.0)
Hepatobiliary disorders								
-Total	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	1(33.3)	1(20.0)	0(0.0)
Hepatic function abnormal	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hepatitis acute	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	1(33.3)	0(0.0)	0(0.0)
Hyperbilirubinaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Immune system disorders								
-Total	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Seasonal allergy	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Infections and infestations								
-Total	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	1(20.0)
Device related infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	1(20.0)
Hepatitis viral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Herpes zoster	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Influenza	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lung infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Nasopharyngitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pseudomembranous colitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Rhinitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Investigations								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	3(100.0)	1(33.3)	4(80.0)	0(0.0)
Alanine aminotransferase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Aspartate aminotransferase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(20.0)	0(0.0)
Blood albumin decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)
Blood alkaline phosphatase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	1(33.3)	1(20.0)	0(0.0)
Blood bilirubin increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Blood creatinine increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Electrocardiogram QT prolonged	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Haemoglobin decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)

Weight decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(66.7)	0(0.0)	0(0.0)	0(0.0)
Weight increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
White blood cell count decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
White blood cell count increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)
Metabolism and nutrition disorders								
-Total	1(33.3)	0(0.0)	1(33.3)	0(0.0)	2(66.7)	0(0.0)	1(20.0)	0(0.0)
Decreased appetite	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Hyperuricaemia	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Hypoalbuminaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Hypokalaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Hypomagnesaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Musculoskeletal and connective tissue disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Arthralgia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Back pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Muscle fatigue	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Musculoskeletal stiffness	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pain in extremity	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Neoplasms benign, malignant and unspecified (including cysts and polyps)								
-Total	1(33.3)	0(0.0)	1(33.3)	0(0.0)	2(66.7)	0(0.0)	2(40.0)	0(0.0)
Cancer pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(66.7)	0(0.0)	0(0.0)	0(0.0)
Tumour associated fever	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)
Tumour pain	1(33.3)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Nervous system disorders								
-Total	1(33.3)	0(0.0)	0(0.0)	0(0.0)	2(66.7)	0(0.0)	2(40.0)	0(0.0)
Dizziness	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dysgeusia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Headache	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(20.0)	0(0.0)
Hypoaesthesia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Neuropathy peripheral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Optic neuritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Peripheral motor neuropathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Peripheral sensory neuropathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Presyncope	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Tension headache	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Psychiatric disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)
Delirium	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Insomnia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Renal and urinary disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Urinary tract obstruction	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Reproductive system and breast disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dysmenorrhoea	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Respiratory, thoracic and mediastinal disorders								
-Total	1(33.3)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)
Cough	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Dyspnoea	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Haemoptysis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Hyperventilation	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Skin and subcutaneous tissue disorders								
-Total	0(0.0)	0(0.0)	3(100.0)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Decubitus ulcer	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dermatitis contact	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dry skin	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pruritus	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Rash	0(0.0)	0(0.0)	2(66.7)	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)
Vascular disorders								
-Total	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)
Hypertension	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)

	AUY922 40 mg/m^2 N=3		**AUY922 54 mg/m^2 N=6**		**AUY922 70 mg/m^2 N=8**		**All patients N=31**	
Primary SOC Preferred term	**All grades n (%)**	**Grade 3/4 n (%)**	**All grades n (%)**	**Grade 3/4 n (%)**	**All grades n (%)**	**Grade 3/4 n (%)**	**All grades n (%)**	**Grade 3/4 n (%)**
Any primary SOC								
-Total	3(100.0)	2(66.7)	6(100.0)	1(16.7)	8(100.0)	2(25.0)	31(100.0)	10(32.3)
Blood and lymphatic system disorders								
-Total	1(33.3)	1(33.3)	2(33.3)	1(16.7)	2(25.0)	1(12.5)	9(29.0)	4(12.9)
Anaemia	1(33.3)	1(33.3)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	4(12.9)	2(6.5)

Lymphopenia	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(12.5)	1(12.5)	4(12.9)	1(3.2)
Neutropenia	0(0.0)	0(0.0)	2(33.3)	1(16.7)	0(0.0)	0(0.0)	2(6.5)	1(3.2)
Cardiac disorders								
-Total	1(33.3)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	3(9.7)	0(0.0)
Atrioventricular block first degree	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Bradycardia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Cardiac discomfort	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Sinus bradycardia	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Ventricular arrhythmia	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Eye disorders								
-Total	2(66.7)	0(0.0)	5(83.3)	0(0.0)	6(75.0)	0(0.0)	18(58.1)	0(0.0)
Cataract	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	2(6.5)	0(0.0)
Conjunctival haemorrhage	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Diplopia	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Eye disorder	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	2(6.5)	0(0.0)
Eye pruritus	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Eyelid oedema	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Glaucoma	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Night blindness	1(33.3)	0(0.0)	5(83.3)	0(0.0)	3(37.5)	0(0.0)	13(41.9)	0(0.0)
Photophobia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Photopsia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Retinopathy	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Vision blurred	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Visual acuity reduced	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Visual impairment	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Vitreous floaters	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Gastrointestinal disorders								
-Total	3(100.0)	0(0.0)	6(100.0)	1(16.7)	8(100.0)	1(12.5)	27(87.1)	3(9.7)
Abdominal pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Abdominal pain upper	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	2(6.5)	0(0.0)
Anal inflammation	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Cheilitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Constipation	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Diarrhoea	2(66.7)	0(0.0)	5(83.3)	1(16.7)	7(87.5)	0(0.0)	20(64.5)	1(3.2)
Dyspepsia	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Frequent bowel movements	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Ileus paralytic	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(12.5)	1(3.2)	1(3.2)
Mallory-Weiss syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)

Nausea	2(66.7)	0(0.0)	2(33.3)	0(0.0)	3(37.5)	0(0.0)	9(29.0)	0(0.0)
Oesophageal fistula	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	1(3.2)
Rectal haemorrhage	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Stomatitis	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	2(6.5)	0(0.0)
Vomiting	1(33.3)	0(0.0)	1(16.7)	0(0.0)	3(37.5)	0(0.0)	5(16.1)	0(0.0)
General disorders and administration site conditions								
-Total	1(33.3)	0(0.0)	4(66.7)	1(16.7)	4(50.0)	0(0.0)	16(51.6)	2(6.5)
Chest discomfort	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	2(6.5)	0(0.0)
Fatigue	0(0.0)	0(0.0)	3(50.0)	1(16.7)	1(12.5)	0(0.0)	9(29.0)	1(3.2)
Influenza like illness	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Injection site pain	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Localised oedema	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Malaise	1(33.3)	0(0.0)	1(16.7)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Oedema peripheral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	2(6.5)	0(0.0)
Pyrexia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	4(12.9)	1(3.2)
Hepatobiliary disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	5(16.1)	1(3.2)
Hepatic function abnormal	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	2(6.5)	0(0.0)
Hepatitis acute	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	1(3.2)
Hyperbilirubinaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	2(6.5)	0(0.0)
Immune system disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Seasonal allergy	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Infections and infestations								
-Total	0(0.0)	0(0.0)	1(16.7)	0(0.0)	3(37.5)	1(12.5)	7(22.6)	2(6.5)
Device related infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	1(3.2)
Hepatitis viral	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Herpes zoster	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Influenza	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Lung infection	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Nasopharyngitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Pseudomembranous colitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(12.5)	1(3.2)	1(3.2)
Rhinitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	2(6.5)	0(0.0)
Investigations								
-Total	0(0.0)	0(0.0)	1(16.7)	1(16.7)	4(50.0)	2(25.0)	12(38.7)	4(12.9)

Alanine aminotransferase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	2(6.5)	0(0.0)
Aspartate aminotransferase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Blood albumin decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Blood alkaline phosphatase increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(12.5)	3(9.7)	2(6.5)
Blood bilirubin increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Blood creatinine increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Electrocardiogram QT prolonged	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Haemoglobin decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(12.5)	2(6.5)	1(3.2)
Weight decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Weight increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
White blood cell count decreased	0(0.0)	0(0.0)	1(16.7)	1(16.7)	0(0.0)	0(0.0)	1(3.2)	1(3.2)
White blood cell count increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Metabolism and nutrition disorders								
-Total	0(0.0)	0(0.0)	1(16.7)	1(16.7)	3(37.5)	0(0.0)	9(29.0)	1(3.2)
Decreased appetite	0(0.0)	0(0.0)	1(16.7)	1(16.7)	3(37.5)	0(0.0)	6(19.4)	1(3.2)
Hyperuricaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Hypoalbuminaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Hypokalaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	2(6.5)	0(0.0)
Hypomagnesaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Musculoskeletal and connective tissue disorders								
-Total	1(33.3)	0(0.0)	0(0.0)	0(0.0)	4(50.0)	0(0.0)	5(16.1)	0(0.0)
Arthralgia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	0(0.0)	2(6.5)	0(0.0)
Back pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Muscle fatigue	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Musculoskeletal stiffness	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Pain in extremity	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Neoplasms benign, malignant and unspecified (including cysts and polyps)								
-Total	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	8(25.8)	0(0.0)
Cancer pain	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	4(12.9)	0(0.0)
Tumour associated fever	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)

Tumour pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Nervous system disorders								
-Total	2(66.7)	1(33.3)	2(33.3)	0(0.0)	4(50.0)	0(0.0)	13(41.9)	1(3.2)
Dizziness	1(33.3)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	1(3.2)
Dysgeusia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Headache	0(0.0)	0(0.0)	0(0.0)	0(0.0)	3(37.5)	0(0.0)	5(16.1)	0(0.0)
Hypoaesthesia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Neuropathy peripheral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Optic neuritis	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(12.5)	0(0.0)	2(6.5)	0(0.0)
Peripheral motor neuropathy	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Peripheral sensory neuropathy	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Presyncope	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Tension headache	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Psychiatric disorders								
-Total	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	3(9.7)	0(0.0)
Delirium	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Insomnia	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Renal and urinary disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Urinary tract obstruction	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Reproductive system and breast disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Dysmenorrhoea	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Respiratory, thoracic and mediastinal disorders								
-Total	1(33.3)	0(0.0)	2(33.3)	0(0.0)	0(0.0)	0(0.0)	7(22.6)	0(0.0)
Cough	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	3(9.7)	0(0.0)
Dyspnoea	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Haemoptysis	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)	0(0.0)
Hyperventilation	0(0.0)	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Skin and subcutaneous tissue disorders								
-Total	1(33.3)	0(0.0)	3(50.0)	0(0.0)	3(37.5)	0(0.0)	11(35.5)	0(0.0)
Decubitus ulcer	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	1(3.2)	0(0.0)
Dermatitis contact	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Dry skin	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)	0(0.0)
Pruritus	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Rash	0(0.0)	0(0.0)	2(33.3)	0(0.0)	1(12.5)	0(0.0)	6(19.4)	0(0.0)

Vascular disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)
Hypertension	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	0(0.0)	3(9.7)	0(0.0)

Primary SOCs are presented alphabetically; preferred terms are sorted within primary SOC alphabetically.

A patient with multiple occurrences of an AE under one treatment group is counted only once in the AE category for that treatment group.

A patient with multiple AEs within a primary SOC is counted only once in the total row.

Frequent AEs (with at least 10 % incidence in any treatment group), regardless of study drug relationship, by primary SOC, preferred term and treatment (safety set)

Primary SOC Preferred term	AUY922 8 mg/m^2 N=3 n (%)	AUY922 16 mg/m^2 N=3 n (%)	AUY922 22 mg/m^2 N=3 n (%)	AUY922 28 mg/m^2 N=5 n (%)	AUY922 40 mg/m^2 N=3 n (%)	AUY922 54 mg/m^2 N=6 n (%)	AUY922 70 mg/m^2 N=8 n (%)	AUY922 All Patients N=31 n (%)
Any primary SOC								
-Total	3(100)	3(100)	3(100)	5(100)	3(100)	6(100)	8(100)	31(100)
Blood and lymphatic system disorders								
-Total	1(33.3)	0(0.0)	0(0.0)	3(60.0)	1(33.3)	2(33.3)	2(25.0)	9(29.0)
Anaemia	1(33.3)	0(0.0)	0(0.0)	1(20.0)	1(33.3)	0(0.0)	1(12.5)	4(12.9)
Lymphopenia	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	1(16.7)	1(12.5)	4(12.9)
Neutropenia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(33.3)	0(0.0)	2(6.5)
Cardiac disorders								
-Total	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(33.3)	1(16.7)	0(0.0)	3(9.7)
Atrioventricular block first degree	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	2(6.5)
Bradycardia	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Cardiac discomfort	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Sinus bradycardia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Ventricular arrhythmia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Eye disorders								
-Total	0(0.0)	0(0.0)	2(66.7)	3(60.0)	2(66.7)	5(83.3)	6(75.0)	18(58.1)
Cataract	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	2(6.5)
Conjunctival haemorrhage	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Diplopia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)
Eye disorder	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	2(6.5)
Eye pruritus	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Eyelid oedema	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)

Glaucoma	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Night blindness	0(0.0)	0(0.0)	2(66.7)	2(40.0)	1(33.3)	5(83.3)	3(37.5)	13(41.9)
Photophobia	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Photopsia	0(0.0)	0(0.0)	1(33.3)	1(20.0)	0(0.0)	0(0.0)	1(12.5)	3(9.7)
Retinopathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Vision blurred	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)
Visual acuity reduced	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Visual impairment	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Vitreous floaters	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)
Gastrointestinal disorders								
-Total	0(0.0)	2(66.7)	3(100)	5(100)	3(100)	6(100)	8(100)	27(87.1)
Abdominal pain	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Abdominal pain upper	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	2(6.5)
Anal inflammation	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Cheilitis	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Constipation	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(33.3)	0(0.0)	1(12.5)	3(9.7)
Diarrhoea	0(0.0)	0(0.0)	2(66.7)	4(80.0)	2(66.7)	5(83.3)	7(87.5)	20(64.5)
Dyspepsia	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	2(6.5)
Frequent bowel movements	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Ileus paralytic	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Mallory-Weiss syndrome	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Nausea	0(0.0)	1(33.3)	0(0.0)	1(20.0)	2(66.7)	2(33.3)	3(37.5)	9(29.0)
Oesophageal fistula	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Rectal haemorrhage	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Stomatitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	1(12.5)	2(6.5)
Vomiting	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	1(16.7)	3(37.5)	5(16.1)
General disorders and administration site conditions								
-Total	1(33.3)	2(66.7)	1(33.3)	3(60.0)	1(33.3)	4(66.7)	4(50.0)	16(51.6)
Chest discomfort	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	2(6.5)
Fatigue	1(33.3)	1(33.3)	1(33.3)	2(40.0)	0(0.0)	3(50.0)	1(12.5)	9(29.0)
Influenza like illness	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Injection site pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Localised oedema	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Malaise	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	1(16.7)	1(12.5)	3(9.7)
Oedema peripheral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	2(6.5)
Pyrexia	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	0(0.0)	2(25.0)	4(12.9)
Hepatobiliary disorders								
-Total	1(33.3)	0(0.0)	1(33.3)	1(20.0)	0(0.0)	0(0.0)	2(25.0)	5(16.1)

Hepatic function abnormal	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	2(6.5)
Hepatitis acute	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Hyperbilirubinaemia	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	1(12.5)	2(6.5)
Immune system disorders								
-Total	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Seasonal allergy	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Infections and infestations								
-Total	1(33.3)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	1(16.7)	3(37.5)	7(22.6)
Device related infection	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Hepatitis viral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Herpes zoster	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Influenza	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Lung infection	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Nasopharyngitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Pseudomembranous colitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Rhinitis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	2(6.5)
Investigations								
-Total	0(0.0)	0(0.0)	3(100)	4(80.0)	0(0.0)	1(16.7)	4(50.0)	12(38.7)
Alanine aminotransferase increased	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	2(6.5)
Aspartate aminotransferase increased	0(0.0)	0(0.0)	1(33.3)	1(20.0)	0(0.0)	0(0.0)	1(12.5)	3(9.7)
Blood albumin decreased	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	0(0.0)	1(12.5)	3(9.7)
Blood alkaline phosphatase increased	0(0.0)	0(0.0)	1(33.3)	1(20.0)	0(0.0)	0(0.0)	1(12.5)	3(9.7)
Blood bilirubin increased	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Blood creatinine increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Electrocardiogram QT prolonged	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Haemoglobin decreased	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	1(12.5)	2(6.5)
Weight decreased	0(0.0)	0(0.0)	2(66.7)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)
Weight increased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
White blood cell count decreased	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)

White blood cell count increased	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	0(0.0)	1(12.5)	3(9.7)
Metabolism and nutrition disorders								
-Total	1(33.3)	1(33.3)	2(66.7)	1(20.0)	0(0.0)	1(16.7)	3(37.5)	9(29.0)
Decreased appetite	0(0.0)	1(33.3)	1(33.3)	0(0.0)	0(0.0)	1(16.7)	3(37.5)	6(19.4)
Hyperuricaemia	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Hypoalbuminaemia	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Hypokalaemia	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	2(6.5)
Hypomagnesaemia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Musculoskeletal and connective tissue disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	4(50.0)	5(16.1)
Arthralgia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(25.0)	2(6.5)
Back pain	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Muscle fatigue	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Musculoskeletal stiffness	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Pain in extremity	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)
Neoplasms benign, malignant and unspecified (including cysts and polyps)								
-Total	1(33.3)	1(33.3)	2(66.7)	2(40.0)	1(33.3)	0(0.0)	1(12.5)	8(25.8)
Cancer pain	0(0.0)	0(0.0)	2(66.7)	0(0.0)	1(33.3)	0(0.0)	1(12.5)	4(12.9)
Tumour associated fever	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)
Tumour pain	1(33.3)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(6.5)
Nervous system disorders								
-Total	1(33.3)	0(0.0)	2(66.7)	2(40.0)	2(66.7)	2(33.3)	4(50.0)	13(41.9)
Dizziness	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)
Dysgeusia	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Headache	0(0.0)	0(0.0)	1(33.3)	1(20.0)	0(0.0)	0(0.0)	3(37.5)	5(16.1)
Hypoaesthesia	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Neuropathy peripheral	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Optic neuritis	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	1(12.5)	2(6.5)
Peripheral motor neuropathy	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)
Peripheral sensory neuropathy	0(0.0)	0(0.0)	0(0.0)	1(20.0)	1(33.3)	0(0.0)	0(0.0)	2(6.5)
Presyncope	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Tension headache	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Psychiatric disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	2(40.0)	0(0.0)	1(16.7)	0(0.0)	3(9.7)
Delirium	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)

Insomnia	0(0.0)	0(0.0)	0(0.0)	1(20.0)	0(0.0)	1(16.7)	0(0.0)	2(6.5)
Renal and urinary disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Urinary tract obstruction	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Reproductive system and breast disorders								
-Total	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Dysmenorrhoea	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Respiratory, thoracic and mediastinal disorders								
-Total	1(33.3)	1(33.3)	0(0.0)	2(40.0)	1(33.3)	2(33.3)	0(0.0)	7(22.6)
Cough	0(0.0)	1(33.3)	0(0.0)	1(20.0)	0(0.0)	1(16.7)	0(0.0)	3(9.7)
Dyspnoea	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Haemoptysis	0(0.0)	0(0.0)	0(0.0)	1(20.0)	1(33.3)	0(0.0)	0(0.0)	2(6.5)
Hyperventilation	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Skin and subcutaneous tissue disorders								
-Total	0(0.0)	3(100)	0(0.0)	1(20.0)	1(33.3)	3(50.0)	3(37.5)	11(35.5)
Decubitus ulcer	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Dermatitis contact	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Dry skin	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)
Pruritus	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(16.7)	1(12.5)	3(9.7)
Rash	0(0.0)	2(66.7)	0(0.0)	1(20.0)	0(0.0)	2(33.3)	1(12.5)	6(19.4)
Vascular disorders								
-Total	0(0.0)	1(33.3)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	3(9.7)
Hypertension	0(0.0)	1(33.3)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	3(9.7)

Primary SOCs are presented alphabetically; preferred terms are sorted within primary SOC alphabetically.

A patient with multiple occurrences of an AE under one treatment group is counted only once in the AE category for that treatment group.

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SAEs, regardless of study drug relationship, by primary SOC and preferred term and treatment (safety set)

Primary system organ class Preferred term	AUY922 22 mg/m^2 N=3 n (%)	AUY922 28 mg/m^2 N=5 n (%)	AUY922 40 mg/m^2 N=3 n (%)	AUY922 54 mg/m^2 N=6 n (%)	AUY922 70 mg/m^2 N=8 n (%)	AUY922 All Patients N=31 n (%)
Any primary system organ class						
-Total	1(33.3)	3(60.0)	1(33.3)	2(33.3)	1(12.5)	8(25.8)
Cardiac disorders						

-Total	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Ventricular arrhythmia	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Gastrointestinal disorders						
-Total	0(0.0)	1(20.0)	0(0.0)	1(16.7)	1(12.5)	3(9.7)
Diarrhoea	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Ileus paralytic	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(12.5)	1(3.2)
Oesophageal fistula	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
General disorders and administration site conditions						
-Total	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Fatigue	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Hepatobiliary disorders						
-Total	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Hepatitis acute	1(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Infections and infestations						
-Total	0(0.0)	2(40.0)	0(0.0)	1(16.7)	0(0.0)	3(9.7)
Device related infection	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Hepatitis viral	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Lung infection	0(0.0)	1(20.0)	0(0.0)	0(0.0)	0(0.0)	1(3.2)
Investigations						
-Total	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Electrocardiogram QT prolonged	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Metabolism and nutrition disorders						
-Total	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Decreased appetite	0(0.0)	0(0.0)	0(0.0)	1(16.7)	0(0.0)	1(3.2)
Nervous system disorders						
-Total	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)
Dizziness	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	1(3.2)

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Other Relevant Findings
Date of Clinical Trial Report 14 Dec 2012
Date Inclusion on Novartis Clinical Trial Results Database 21 Feb 2013
Date of Latest Update