

THE LANCET Oncology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Seddon B, Strauss SJ, Whelan J, et al. Gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas (GeDDiS): a randomised controlled phase 3 trial. *Lancet Oncol* 2017; published online Sept 4. [http://dx.doi.org/10.1016/S1470-2045\(17\)30622-8](http://dx.doi.org/10.1016/S1470-2045(17)30622-8).

Appendix Table 1. Recruiting investigator sites

Site	Investigator	Number of patients
University College Hospital, London	Dr Beatrice Seddon	48
The Royal Marsden Hospital, London	Prof Ian Judson	34
The Christie Hospital, Manchester	Dr Michael Leahy	32
Clatterbridge Centre for Oncology, Bebington	Dr Nasim Ali	19
St James's University Hospital, Leeds	Dr Maria Marples	17
Weston Park Hospital, Sheffield	Prof Penella Woll	14
Beatson West of Scotland Cancer Centre, Glasgow	Dr Fiona Cowie	12
Kantonsspital, St Gallen, Switzerland	Dr Christian Rothermundt	8
Western General Hospital; Edinburgh	Dr Richard Hayward	8
Belfast City Hospital	Dr Heather McCarty	7
Bristol Haematology & Oncology Centre	Dr Adam Dangoor	7
Nottingham University Hospital	Dr Ivo Hennig	6
Singleton Hospital, Swansea	Prof John Wagstaff	6
Cheltenham General Hospital	Dr Charles Candish	5
Northampton General Hospital	Dr Craig Mcmillan	5
Queen Elizabeth Hospital, Birmingham	Dr David Peake	5
Royal Derby Hospital	Dr Mojca Persic	5
Addenbrookes Hospital, Cambridge	Dr Helena Earl	3
Churchill Hospital	Prof Andrew Hassan	3
Leicester Royal Infirmary	Dr Samreen Ahmed	3
Norfolk & Norwich University Hospital	Dr Helen Stubbings	3
Royal Devon and Exeter Hospital	Dr Mark Napier	3
Ninewells Hospital, Dundee	Dr Michelle Ferguson	2
Aberdeen Royal Infirmary	Dr Radha Todd	1
Castle Hill Hospital	Prof Michael Lind	1

Appendix Table 2. ‘Other’ sarcoma subtypes

Type	Dox (N=129)	GemDoc (N=128)
Pre-listed options on CRF		
Non-uterine leiomyosarcoma	18 (14.0%)	21 (16.4%)
Dedifferentiated liposarcoma	7 (5.4%)	5 (3.9%)
Spindle cell sarcoma with myofibroblastic differentiation/high grade	4 (3.1%)	5 (3.9%)
Myxoid and round cell liposarcoma	7 (5.4%)	2 (1.6%)
Myxofibrosarcoma	4 (3.1%)	4 (3.1%)
Malignant peripheral nerve sheath tumour	5 (3.9%)	2 (1.6%)
Angiosarcoma	3 (2.3%)	4 (3.1%)
Epithelioid sarcoma	3 (2.3%)	1 (0.8%)
Malignant solitary fibrous tumour (>4 mitoses/10 hpf)	0	3 (2.3%)
Fibrosarcoma	1 (0.8%)	1 (0.8%)
Malignant fibrous histiocytoma	1 (0.8%)	1 (0.8%)
Sarcoma NOS	0	2 (1.6%)
Clear cell sarcoma	1 (0.8%)	0
Entered as free text on CRF		
Endometrial stromal sarcoma (high grade)	0	1 (0.8%)
Endometrial stromal sarcoma of the endometrium	0	1 (0.8%)
Haemangiopericytoma	0	1 (0.8%)
Leiomyosarcoma	4 (3.1%)	0
Liposarcoma	0	2 (1.6%)
Liposarcoma well-differentiated	1 (0.8%)	0
Metastatic leiomyosarcoma	1 (0.8%)	2 (1.6%)
Undifferentiated pleomorphic spindle cell sarcoma, grade 3	0	1 (0.8%)
Undifferentiated spindle cell sarcoma	1 (0.8%)	0
Undifferentiated spindle and round cell sarcoma	0	1 (0.8%)
Adenosarcoma of uterine origin	0	1 (0.8%)
Endometrial sarcoma	0	1 (0.8%)
High grade endometrial stromal sarcoma	1 (0.8%)	0
High grade leiomyosarcoma in the mesentery of small intestine	1 (0.8%)	0
High grade leiomyosarcoma	1 (0.8%)	0
High grade pleomorphic spindle cell sarcoma, not otherwise specified, grade 3	0	1 (0.8%)
High grade undifferentiated sarcoma	2 (1.6%)	0
Intimal sarcoma	0	1 (0.8%)
Liposarcoma myxoid round cell grade 3	0	1 (0.8%)
Myosarcoma	1 (0.8%)	0
Peripheral nerve sheath tumour	0	1 (0.8%)
Pleomorphic myxoid liposarcoma	0	1 (0.8%)
Poorly differentiated liposarcoma	1 (0.8%)	0
Retroperitoneal leiomyosarcoma	0	1 (0.8%)
Retroperitoneal sarcoma	1 (0.8%)	0
Spindle cell sarcoma most in keeping with a malignant peripheral nerve sheath tumour	0	1 (0.8%)
Undifferentiated myxoid endometrial sarcoma	0	1 (0.8%)
Well-differentiated and de-differentiated liposarcoma with myxofibrosarcomatous and chondrosarcoma elements	1 (0.8%)	0
Sarcoma (type not specified on CRF)	1 (0.8%)	0

Appendix Table 3. Central pathology review – major and minor discrepancies

Trial ID	Local histology	Central review histology	Discrepancy type
GEDD087	Pleomorphic sarcoma	Leiomyosarcoma- non-uterine	Major
GEDD112	Epithelioid sarcoma	Leiomyosarcoma - non-uterine	Major
GEDD144	Pleomorphic sarcoma	Leiomyosarcoma - non-uterine	Major
GEDD160	Other eligible sarcomas (Non-uterine leiomyosarcoma)	Pleomorphic sarcoma/malignant fibrous histiocytoma	Major
GEDD184	Other eligible sarcomas (Non-uterine leiomyosarcoma)	Pleomorphic sarcoma/malignant fibrous histiocytoma	Major
GEDD205	Other eligible sarcomas (retroperitoneal sarcoma)	Leiomyosarcoma - non-uterine	Major
GEDD226	Spindle cell sarcoma with myofibroblastic differentiation/high grade	Leiomyosarcoma - non-uterine	Major
GEDD008	Dedifferentiated liposarcoma	Pleomorphic sarcoma/malignant fibrous histiocytoma	Major
GEDD016	Sarcoma NOS	Spindle cell sarcoma with myofibroblastic differentiation/myofibrosarcoma - (intermediate and high grade)	Major
GEDD018	spindle cell sarcoma most in keeping with a malignant peripheral nerve sheath tumour	Sarcoma NOS	Major
GEDD023	Pleomorphic sarcoma	pleomorphic liposarcoma	Major
GEDD025	Other eligible sarcomas (Non-uterine leiomyosarcoma)	Pleomorphic sarcoma/malignant fibrous histiocytoma	Major
GEDD036	Dedifferentiated liposarcoma	Malignant solitary fibrous tumour (>4 mitoses /10 hpf)	Major
GEDD049	Fibrosarcoma	Spindle cell sarcoma, NOS	Major
GEDD070	Pleomorphic sarcoma	Malignant solitary fibrous tumour (>4 mitoses /10 hpf)	Major
GEDD077	Myxoid and round cell liposarcoma	Myxofibrosarcoma	Major
GEDD080	Other eligible sarcomas (not specified on CRF)	Epithelioid sarcoma	Major
GEDD086	Myxofibrosarcoma	Other (specify) - Sclerosing epithelioid fibrosarcoma	Major
GEDD109	Liposarcoma	Sarcoma NOS	Major
GEDD117	Poorly differentiated liposarcoma	Pleomorphic sarcoma/malignant fibrous histiocytoma	Major
GEDD129	Undifferentiated spindle cell sarcoma	Myxofibrosarcoma	Major
GEDD139	Haemangiopericytoma	Sarcoma NOS	Major
GEDD147	Spindle cell sarcoma with myofibroblastic differentiation/high grade	Malignant peripheral nerve sheath tumour	Major
GEDD151	Spindle cell sarcoma with myofibroblastic differentiation/high grade	Myxofibrosarcoma	Major
GEDD155	Myxoid and round cell liposarcoma	Sarcoma NOS	Major
GEDD169	Malignant peripheral nerve sheath tumour	Sarcoma NOS	Major
GEDD181	Pleomorphic sarcoma	Myxofibrosarcoma	Major
GEDD203	Intimal sarcoma	Angiosarcoma	Major
GEDD208	High grade undifferentiated sarcoma	Malignant peripheral nerve sheath tumour	Major
GEDD215	Angiosarcoma	Sarcoma NOS	Major
GEDD224	Pleomorphic sarcoma	Other (specify) - Malignant uterine pecoma	Major
GEDD225	Pleomorphic sarcoma	Myxofibrosarcoma	Major
GEDD255	Malignant peripheral nerve sheath tumour	Sarcoma NOS	Major
GEDD059	Undifferentiated endometrial sarcoma	Adenosarcoma with sarcomatous overgrowth	Major
GEDD092	Initial - Other eligible sarcomas (Non-uterine leiomyosarcoma). Local review - GIST ¹	GIST (CD117 positive)	Major (ineligible)
GEDD199	Malignant solitary fibrous tumour (>4 mitoses/10 hpf) ²	Extra-skeletal myxoid chondrosarcoma	Major (ineligible)
GEDD013	Spindle cell sarcoma with myofibroblastic differentiation/high grade	Pleomorphic sarcoma/malignant fibrous histiocytoma	Minor
GEDD033	Pleomorphic sarcoma	Spindle cell sarcoma with myofibroblastic differentiation/myofibrosarcoma - (intermediate and high grade)	Minor

Trial ID	Local histology	Central review histology	Discrepancy type
GEDD113	Spindle cell sarcoma with myofibroblastic differentiation/high grade	Pleomorphic sarcoma/malignant fibrous histiocytoma	Minor
GEDD118	Myxofibrosarcoma	Pleomorphic sarcoma/malignant fibrous histiocytoma	Minor
GEDD127	Myxofibrosarcoma	Sarcoma NOS	Minor
GEDD140	Grade 2 liposarcoma	Dedifferentiated liposarcoma	Minor
GEDD141	Pleomorphic sarcoma	Other (specify) - High Grade Uterine Sarcoma, NOS	Minor
GEDD149	Pleomorphic sarcoma	Sarcoma NOS	Minor
GEDD150	Myosarcoma	Spindle cell sarcoma with myofibroblastic differentiation/ myofibrosarcoma - (intermediate and high grade)	Minor
GEDD163	Undifferentiated spine and round cell sarcoma	Sarcoma NOS	Minor
GEDD168	Liposarcoma well differentiated	Dedifferentiated liposarcoma	Minor
GEDD197	Spindle cell sarcoma with myofibroblastic differentiation/high grade	Myxofibrosarcoma	Minor
GEDD209	Pleomorphic sarcoma	Sarcoma NOS	Minor
GEDD227	Pleomorphic sarcoma	Spindle cell sarcoma with myofibroblastic differentiation/ myofibrosarcoma - (intermediate and high grade)	Minor
GEDD259	Spindle cell sarcoma with myofibroblastic differentiation/high grade	Pleomorphic sarcoma/malignant fibrous histiocytoma	Minor

¹ Patient withdrawn from trial by site following review of pathology and diagnosis of GIST (included in ITT analysis)

² Patient classified as ineligible on central review of pathology (included in ITT analysis)

Appendix Table 4. Chemotherapy cycles received

Cycle		Dox (N=129)	Gem (N=128)	Doc (N=128)
1	Started	128 (99.2%)	126 (98.4%)	118 (92.2%)
	Did not complete	0	8 (6.3%)	1 (0.8%)
2	Started	118 (91.5%)	110 (85.9%)	106 (82.8%)
	Did not complete	1 (0.8%)	7 (6.4%)	4 (3.8%)
3	Started	100 (77.5%)	89 (69.5%)	87 (68.0%)
	Did not complete	0	5 (5.6%)	3 (3.4%)
4	Started	95 (73.6%)	75 (58.6%)	71 (55.5%)
	Did not complete	0	6 (8.0%)	2 (2.8%)
5	Started	79 (61.2%)	59 (46.1%)	53 (41.4%)
	Did not complete	0	8 (13.6%)	2 (3.8%)
6	Started	71 (55.0%)	52 (40.6%)	49 (38.3%)
	Did not complete	0	3 (5.8%)	0 (0.0%)

Appendix Table 5. Reason for withdrawal from treatment

Reason¹	Dox (N=129)	GemDoc (N=128)
Disease progression	34	39
Serious adverse event	2	2
Unacceptable toxicity	1	13
Clinician decision	5	5
Death	5	4
Symptomatic deterioration	4	3
Intercurrent illness preventing further treatment	1	1
Patient decision ²	1	2
Other	5	9
Unknown	0	1
Total	58	79

Notes:

1. Participants who did not start treatment are included in this table.
2. Includes one participant in each arm who withdrew consent

Appendix Table 6. SAEs by grade and treatment arm. Data are N (% within treatment arm by SAE)

Grade	Dox					GemDoc				
	1 or 2	3	4	5	Total	1 or 2	3	4	5	Total
Abdominal pain	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	3 (50.0%)	3 (50.0%)	0 (0.0%)	0 (0.0%)	6
Anemia	3 (50.0%)	3 (50.0%)	0 (0.0%)	0 (0.0%)	6	2 (50.0%)	1 (25.0%)	1 (25.0%)	0 (0.0%)	4
Anorectal infection	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Ascites	0	0	0	0	0	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	2
Back pain	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Bloating	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Blood bilirubin increased	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Bronchial infection	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	2
Catheter related infection	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Chest pain - cardiac	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Colonic ulcer	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Confusion	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Constipation	4 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Cough	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Diarrhea	2 (33.3%)	4 (66.7%)	0 (0.0%)	0 (0.0%)	6	3 (33.3%)	5 (55.6%)	1 (11.1%)	0 (0.0%)	9
Dyspepsia	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Dyspnea	0 (0.0%)	5 (100.0%)	0 (0.0%)	0 (0.0%)	5	1 (20.0%)	3 (60.0%)	1 (20.0%)	0 (0.0%)	5
Edema limbs	0	0	0	0	0	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2
Esophageal hemorrhage	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Fatigue	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	2	0	0	0	0	0
Febrile neutropenia	0 (0.0%)	26 (96.3%)	1 (3.7%)	0 (0.0%)	27	0 (0.0%)	13 (86.7%)	2 (13.3%)	0 (0.0%)	15
Female genital tract fistula	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Fever	17 (94.4%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	18	19 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	19
Gastrointestinal disorders, other: diverticulitis	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Gastrointestinal disorders, other: oral thrush	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Heart failure	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0

Grade	Dox					GemDoc				
	1 or 2	3	4	5	Total	1 or 2	3	4	5	Total
Hot flashes	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Hypercalcemia	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1	0	0	0	0	0
Hypokalemia	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Infections and infestations, other: NOS	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	2
Infections and infestations, other: e-coli infection at tumour site	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Infections and infestations, other: gastrointestinal	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Infections and infestations, other: hickman line	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	2	0	0	0	0	0
Infections and infestations, other: source unknown	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Infections and infestations, other: varicella zoster	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1	0	0	0	0	0
Infections and infestations, other: viral	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Left ventricular systolic dysfunction	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Lung infection	0 (0.0%)	6 (100.0%)	0 (0.0%)	0 (0.0%)	6	1 (20.0%)	3 (60.0%)	1 (20.0%)	0 (0.0%)	5
Myalgia	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Nail infection	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Nausea	3 (75.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	4	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	2
Neutrophil count decreased	2 (9.1%)	8 (36.4%)	12 (54.5%)	0 (0.0%)	22	2 (20.0%)	5 (50.0%)	3 (30.0%)	0 (0.0%)	10
Non-cardiac chest pain	3 (75.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	4	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2
Pain	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Pain in extremity	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Palpitations	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Pelvic pain	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Pharyngitis	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Pleuritic pain	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Pneumonitis	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Pneumothorax	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Seizure	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0

Grade	Dox					GemDoc				
	1 or 2	3	4	5	Total	1 or 2	3	4	5	Total
Sepsis	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	2	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1
Skin and subcutaneous tissue disorders, other: cellulitis	0	0	0	0	0	0 (0.0%)	3 (100.0%)	0 (0.0%)	0 (0.0%)	3
Skin and subcutaneous tissue disorders, other: hickman line	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Skin infection	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	1 (33.3%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	3
Skin ulceration	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Small intestinal obstruction	0	0	0	0	0	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1
Sudden death NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1
Syncope	0 (0.0%)	2 (100.0%)	0 (0.0%)	0 (0.0%)	2	0	0	0	0	0
Thromboembolic event	1 (11.1%)	6 (66.7%)	2 (22.2%)	0 (0.0%)	9	0 (0.0%)	2 (50.0%)	2 (50.0%)	0 (0.0%)	4
Tremor	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Tumor pain	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0	0	0	0	0
Upper respiratory infection	1 (33.3%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	3	2 (66.7%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	3
Urinary retention	0	0	0	0	0	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Urinary tract infection	0	0	0	0	0	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	2
Vomiting	1 (33.3%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	3	4 (80.0%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	5
Wound infection	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1

Appendix Table 7. Causes of death.

	Dox (N=74)	GemDoc (N=80)
Disease progression	67 (90.5%)	76 (95.0%)
Combination of disease & treatment	1 (1.4%)	1 (1.3%)
Cardiac death	2 (2.7%)	0 (0.0%)
Other	4 (5.4%) ¹	3 (3.8%) ²

¹. The 4 “other” causes of death in Dox are:

1. Multiorgan failure. Community acquired pneumonia. Metastatic angiosarcoma spleen
2. deep vein thrombosis
3. Intracerebral bleed
4. Unknown, patient died suddenly at home

². The 3 “other” causes of death in GemDoc are:

1. Sudden death, no cause identified
2. Pulmonary embolism, Metastatic leiomyosarcoma
3. Pulmonary embolism due to abdominal sarcoma

Appendix Table 8. Subgroup analyses (based on local histology diagnosis at baseline)

Variable	Value	Treatment HR	Interaction p-value
Sex	Male (N=101)	1.82 (1.19, 2.80) *	0.03
	Female (N=156)	1.01 (0.72, 1.40) *	
Uterine leiomyosarcoma	Other sarcomas (N=186)	1.37 (1.01, 1.85)	0.38
	Uterine leiomyosarcoma (N=71)	1.06 (0.65, 1.72)	
Leiomyosarcoma	Other sarcomas (N=139)	1.56 (1.10, 2.21)	0.14
	Leiomyosarcoma (N=118)	1.06 (0.73, 1.55)	
Histology	Uterine leiomyosarcoma (N=71)	1.06 (0.65, 1.72)	0.24
	Synovial sarcoma (N=11)	4.15 (1.16, 14.85)	
	Pleomorphic sarcoma (N=32)	1.00 (0.48, 2.08)	
	Other eligible sarcomas (N=143)	1.32 (0.94, 1.86)	

* Adjusted for histological subtype

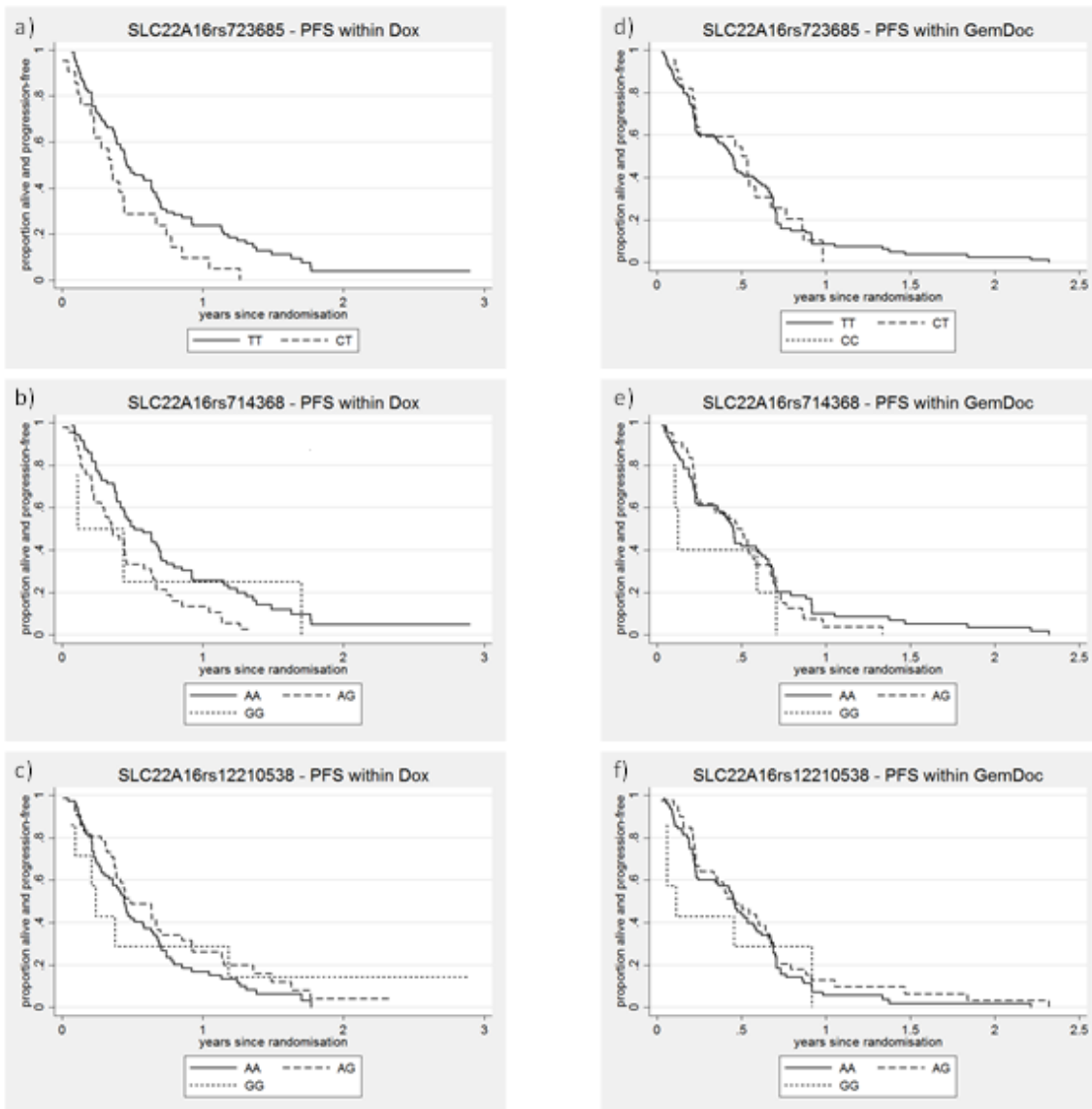
Appendix Table 9. PFS and OS associated with SNPs predicted to have an impact on the pharmacology of Dox (blue), Doc (yellow) and Gem (orange)

Drug	Gene	SNP	Taqman Assay	Allele	Dox		Allele	Gem/Doc	
					HR	OS		HR	OS
Doxorubicin	ABCB1	rs1045642	C__7586657_20	TT (N=28)	1.00 (., .)	1.00 (., .)	TT (N=30)	1.00 (., .)	1.00 (., .)
				CT (N=66)	0.92 (0.58, 1.46)	0.76 (0.42, 1.39)	CT (N=68)	1.62 (1.03, 2.54)	1.25 (0.72, 2.17)
				CC (N=25)	1.30 (0.74, 2.29)	1.48 (0.74, 2.94)	CC (N=23)	1.87 (1.06, 3.31)	1.12 (0.56, 2.27)
		rs1128503	C__7586662_10	CC (N=46)	1.00 (., .)	1.00 (., .)	CC (N=36)	1.00 (., .)	1.00 (., .)
				CT (N=54)	0.74 (0.49, 1.13)	0.79 (0.46, 1.34)	CT (N=62)	0.84 (0.55, 1.28)	1.36 (0.80, 2.30)
				TT (N=19)	1.01 (0.58, 1.77)	1.50 (0.76, 2.94)	TT (N=23)	0.67 (0.39, 1.14)	1.12 (0.58, 2.16)
		rs2032582	C_11711720D_40 & C_11711720C_30	GG (N=42)	1.00 (., .)	1.00 (., .)	GG (N=30)	1.00 (., .)	1.00 (., .)
				GT (N=53)	0.76 (0.49, 1.16)	0.73 (0.42, 1.26)	GT (N=61)	0.72 (0.46, 1.13)	1.39 (0.79, 2.45)
				GA (N=4)	0.48 (0.15, 1.57)	0.37 (0.05, 2.75)	GA (N=6)	0.53 (0.22, 1.30)	1.02 (0.34, 3.01)
	TA (N=2)			0.69 (0.17, 2.86)	0.95 (0.22, 4.05)	TA (N=2)	0.86 (0.20, 3.61)	0.69 (0.09, 5.22)	
	GSTP1	rs1695	C__3237198_20	TT (N=17)	0.88 (0.49, 1.57)	1.12 (0.55, 2.27)	TT (N=22)	0.53 (0.30, 0.95)	0.99 (0.48, 2.02)
				AA (N=59)	1.00 (., .)	1.00 (., .)	AA (N=55)	1.00 (., .)	1.00 (., .)
				AG (N=46)	1.14 (0.76, 1.72)	1.13 (0.68, 1.86)	AG (N=49)	1.10 (0.74, 1.63)	1.04 (0.64, 1.70)
	SLC22A16	rs12210538	C__22271871_10	GG (N=14)	1.21 (0.67, 2.19)	0.62 (0.26, 1.48)	GG (N=17)	1.14 (0.65, 2.00)	1.17 (0.58, 2.37)
				AA (N=71)	1.00 (., .)	1.00 (., .)	AA (N=75)	1.00 (., .)	1.00 (., .)
				AG (N=41)	0.77 (0.51, 1.16)	1.17 (0.71, 1.94)	AG (N=39)	0.84 (0.57, 1.26)	0.96 (0.58, 1.57)
		rs714368 & rs6907567	C__2256675_10 & C__22272571_10	GG (N=7)	0.84 (0.36, 1.98)	0.75 (0.23, 2.47)	GG (N=7)	1.39 (0.60, 3.22)	1.12 (0.45, 2.84)
				AA (N=70)	1.00 (., .)	1.00 (., .)	AA (N=74)	1.00 (., .)	1.00 (., .)
				AG (N=45)	1.75 (1.16, 2.62)	1.36 (0.83, 2.22)	AG (N=42)	1.11 (0.75, 1.64)	1.04 (0.64, 1.67)
		rs723685	C__2953081_10	GG (N=4)	1.33 (0.48, 3.71)	0.40 (0.05, 2.92)	GG (N=5)	1.75 (0.70, 4.38)	1.10 (0.34, 3.54)
TT (N=98)				1.00 (., .)	1.00 (., .)	TT (N=98)	1.00 (., .)	1.00 (., .)	
CT (N=21)				1.72 (1.06, 2.79)	0.89 (0.47, 1.66)	CT (N=22)	0.98 (0.60, 1.59)	0.83 (0.45, 1.51)	
NQ01		rs1800566	C__2091255_30	CC (N=0)	., .)	., .)	CC (N=1)	1.00 (0.14, 7.24)	0.00 (0.00, .)
				CC (N=71)	1.00 (., .)	1.00 (., .)	CC (N=79)	1.00 (., .)	1.00 (., .)
				CT (N=42)	1.31 (0.88, 1.97)	0.85 (0.51, 1.42)	CT (N=36)	1.03 (0.68, 1.55)	1.00 (0.59, 1.68)
NQ02	rs1143684	C__8774861_1_	TT (N=6)	0.50 (0.20, 1.26)	0.56 (0.17, 1.82)	TT (N=6)	0.69 (0.30, 1.59)	1.42 (0.60, 3.32)	
			TT (N=71)	1.00 (., .)	1.00 (., .)	TT (N=67)	1.00 (., .)	1.00 (., .)	
			CT (N=43)	1.30 (0.87, 1.93)	0.82 (0.47, 1.40)	CT (N=46)	1.35 (0.91, 2.01)	1.40 (0.88, 2.23)	
CBR1	rs9024	C__2440206_1_	CC (N=5)	1.08 (0.43, 2.69)	0.86 (0.31, 2.40)	CC (N=8)	1.51 (0.72, 3.17)	1.01 (0.36, 2.85)	
			GG (N=96)	1.00 (., .)	1.00 (., .)	GG (N=89)	1.00 (., .)	1.00 (., .)	
			AG (N=21)	0.85 (0.51, 1.43)	1.28 (0.69, 2.35)	AG (N=30)	0.85 (0.55, 1.30)	0.90 (0.53, 1.51)	
CBR3	rs1056892	C__9483603_10	AA (N=2)	1.33 (0.32, 5.42)	3.28 (0.79, 13.63)	AA (N=2)	0.62 (0.15, 2.52)	0.60 (0.08, 4.34)	
			GG (N=55)	1.00 (., .)	1.00 (., .)	GG (N=45)	1.00 (., .)	1.00 (., .)	
			AG (N=49)	1.23 (0.82, 1.85)	1.00 (0.60, 1.68)	AG (N=57)	1.35 (0.89, 2.04)	1.38 (0.84, 2.26)	
				AA (N=15)	1.73 (0.96, 3.11)	1.25 (0.59, 2.63)	AA (N=19)	1.29 (0.74, 2.22)	0.74 (0.36, 1.55)

Drug	Gene	SNP	Taqman Assay	Allele	Dox		Gem/Doc			
					HR	OS	Allele	PFS		OS
								HR	HR	
Docetaxel	CYP3A41b	rs2740574	C__1837671_50	AA (N=107)	1.00 (., .)	1.00 (., .)	AA (N=111)	1.00 (., .)	1.00 (., .)	
				AG (N=10)	1.14 (0.57, 2.27)	1.73 (0.79, 3.79)	AG (N=8)	1.19 (0.57, 2.45)	0.46 (0.15, 1.47)	
				GG (N=2)	1.35 (0.33, 5.50)	1.04 (0.14, 7.56)	GG (N=2)	1.42 (0.35, 5.82)	2.28 (0.55, 9.46)	
	CYP1B	rs1056836	C__3099976_30	CC (N=20)	1.00 (., .)	1.00 (., .)	CC (N=28)	1.00 (., .)	1.00 (., .)	
				CG (N=65)	1.04 (0.61, 1.76)	1.08 (0.57, 2.03)	CG (N=59)	0.63 (0.39, 1.02)	0.68 (0.40, 1.17)	
				GG (N=34)	0.75 (0.41, 1.36)	0.67 (0.32, 1.42)	GG (N=34)	0.91 (0.55, 1.51)	0.53 (0.29, 0.98)	
	SLCO1B3	rs7311358	C__25765587_40	AA (N=85)	1.00 (., .)	1.00 (., .)	AA (N=87)	1.00 (., .)	1.00 (., .)	
				AG (N=26)	1.14 (0.71, 1.83)	0.93 (0.51, 1.72)	AG (N=29)	1.18 (0.76, 1.83)	1.20 (0.71, 2.03)	
				GG (N=8)	0.98 (0.47, 2.04)	0.96 (0.35, 2.67)	GG (N=5)	0.87 (0.35, 2.15)	1.40 (0.50, 3.89)	
	XRCC4	rs1382368	C__3098143_10	AA (N=86)	1.00 (., .)	1.00 (., .)	AA (N=88)	1.00 (., .)	1.00 (., .)	
				AG (N=27)	1.03 (0.65, 1.62)	0.81 (0.44, 1.49)	AG (N=30)	1.04 (0.67, 1.60)	1.28 (0.77, 2.12)	
				GG (N=6)	1.13 (0.49, 2.59)	1.49 (0.54, 4.15)	GG (N=3)	2.16 (0.68, 6.92)	0.48 (0.07, 3.47)	
	PRDX4	rs518329	C__590682_20	GG (N=36)	1.00 (., .)	1.00 (., .)	GG (N=41)	1.00 (., .)	1.00 (., .)	
				AG (N=61)	0.78 (0.50, 1.21)	1.09 (0.62, 1.90)	AG (N=57)	0.83 (0.55, 1.26)	0.85 (0.51, 1.42)	
				AA (N=22)	0.91 (0.52, 1.62)	1.23 (0.61, 2.49)	AA (N=23)	0.72 (0.42, 1.22)	0.63 (0.32, 1.24)	
	PRDX4	rs518329	C__590682_20	GG or G- (N=44)	1.00 (., .)	1.00 (., .)	GG or G- (N=49)	1.00 (., .)	1.00 (., .)	
				AG (N=43)	1.27 (0.81, 1.98)	0.89 (0.52, 1.51)	AG (N=35)	0.71 (0.45, 1.12)	0.78 (0.45, 1.38)	
				AA or A- (N=32)	0.73 (0.45, 1.21)	0.43 (0.22, 0.85)	AA or A- (N=37)	0.85 (0.55, 1.32)	0.97 (0.57, 1.66)	

Drug	Gene	SNP	Taqman Assay	Allele	Dox		Allele	Gem/Doc	
					PFS	OS		PFS	OS
					HR	HR		HR	HR
Gemcitabine	CDA	rs1048977	C__7477307_30	CC (N=53)	1.00 (., .)	1.00 (., .)	CC (N=54)	1.00 (., .)	1.00 (., .)
				CT (N=47)	1.11 (0.73, 1.69)	1.08 (0.64, 1.82)	CT (N=58)	0.87 (0.60, 1.28)	0.72 (0.45, 1.16)
				TT (N=19)	1.00 (0.58, 1.73)	0.83 (0.39, 1.77)	TT (N=9)	0.99 (0.47, 2.09)	1.19 (0.50, 2.84)
		rs2072671	C__25472931_20	AA (N=57)	1.00 (., .)	1.00 (., .)	AA (N=64)	1.00 (., .)	1.00 (., .)
				AC (N=52)	0.87 (0.58, 1.31)	0.59 (0.35, 0.98)	AC (N=42)	1.20 (0.80, 1.79)	1.44 (0.88, 2.36)
				CC (N=10)	1.28 (0.65, 2.53)	1.00 (0.44, 2.27)	CC (N=15)	0.97 (0.53, 1.77)	2.34 (1.17, 4.70)
	RRM1	rs9937	C__2769876_20	AA (N=30)	1.00 (., .)	1.00 (., .)	AA (N=31)	1.00 (., .)	1.00 (., .)
				AG (N=64)	0.92 (0.58, 1.45)	0.60 (0.35, 1.05)	AG (N=60)	1.03 (0.66, 1.61)	1.28 (0.72, 2.27)
				GG (N=25)	1.04 (0.60, 1.80)	0.69 (0.36, 1.33)	GG (N=30)	1.49 (0.89, 2.51)	1.64 (0.86, 3.15)
	NT5C2	rs11598702	C__11196884_20	TT (N=45)	1.00 (., .)	1.00 (., .)	TT (N=46)	1.00 (., .)	1.00 (., .)
				CT (N=53)	1.01 (0.66, 1.55)	0.74 (0.44, 1.25)	CT (N=56)	1.18 (0.79, 1.77)	1.63 (0.98, 2.72)
				CC (N=21)	1.19 (0.70, 2.05)	0.78 (0.39, 1.56)	CC (N=19)	1.11 (0.65, 1.91)	1.72 (0.89, 3.30)
	CMPK1	rs4492666	C__26214800_10	CC (N=33)	1.00 (., .)	1.00 (., .)	CC (N=33)	1.00 (., .)	1.00 (., .)
				AC (N=61)	1.22 (0.77, 1.92)	1.06 (0.59, 1.87)	AC (N=60)	0.97 (0.63, 1.50)	0.53 (0.31, 0.89)
				AA (N=25)	0.86 (0.48, 1.53)	0.65 (0.31, 1.36)	AA (N=28)	1.04 (0.62, 1.75)	0.56 (0.30, 1.05)
	rs11211524	C__308477_10	AA (N=70)	1.00 (., .)	1.00 (., .)	AA (N=73)	1.00 (., .)	1.00 (., .)	
			AC (N=47)	1.00 (0.68, 1.48)	1.09 (0.67, 1.80)	AC (N=42)	1.13 (0.77, 1.67)	0.99 (0.61, 1.62)	
			CC (N=2)	0.55 (0.08, 4.00)	2.30 (0.31, 17.02)	CC (N=6)	0.70 (0.30, 1.61)	1.11 (0.44, 2.81)	
	DCK	rs4694362	C__11221912_10	TT (N=45)	1.00 (., .)	1.00 (., .)	TT (N=44)	1.00 (., .)	1.00 (., .)
				CT (N=54)	0.94 (0.62, 1.42)	1.36 (0.80, 2.32)	CT (N=59)	1.21 (0.80, 1.81)	1.10 (0.67, 1.82)
CC (N=20)				0.78 (0.43, 1.39)	0.91 (0.42, 1.97)	CC (N=18)	1.05 (0.60, 1.84)	0.95 (0.45, 1.97)	
SLC28A3	rs7867504	C__11764222_20	TT (N=55)	1.00 (., .)	1.00 (., .)	TT (N=53)	1.00 (., .)	1.00 (., .)	
			TC (N=50)	1.03 (0.68, 1.55)	1.10 (0.66, 1.84)	TC (N=61)	1.03 (0.70, 1.51)	1.14 (0.72, 1.81)	
			CC (N=14)	1.02 (0.56, 1.85)	1.52 (0.71, 3.24)	CC (N=7)	0.72 (0.32, 1.59)	0.17 (0.02, 1.25)	
SLC29A1	rs9394992	C__2334579_10	CC (N=67)	1.00 (., .)	1.00 (., .)	CC (N=61)	1.00 (., .)	1.00 (., .)	
			CT (N=44)	1.89 (1.25, 2.86)	1.14 (0.68, 1.89)	CT (N=51)	1.04 (0.71, 1.52)	1.11 (0.68, 1.81)	
			TT (N=8)	1.92 (0.87, 4.26)	1.64 (0.58, 4.65)	TT (N=9)	1.92 (0.94, 3.94)	1.86 (0.86, 4.04)	
rs760370	C__2735230_10	AA (N=40)	1.00 (., .)	1.00 (., .)	AA (N=50)	1.00 (., .)	1.00 (., .)		
		AG (N=56)	0.89 (0.58, 1.38)	0.80 (0.47, 1.38)	AG (N=56)	0.86 (0.58, 1.28)	1.02 (0.63, 1.65)		
		GG (N=23)	1.44 (0.84, 2.46)	0.98 (0.49, 1.94)	GG (N=15)	1.01 (0.56, 1.81)	1.19 (0.57, 2.51)		

Appendix Figure 1: Kaplan Meier plots of PFS of groups selected according to genetic variants in the SLC22A16 gene in the Dox arm (a, b, & c) and the GemDoc arm (d, e & f). P values obtained using a Likelihood ratio test.



Appendix Table 10. Frequency distribution of second line treatment

	Dox (N=62)	GemDoc (N=77*)	Total (%)
Doxorubicin	1	60	61 (42.1%)
Gemcitabine and docetaxel	18	1	19 (13.1%)
Ifosfamide	15	2	17 (11.7%)
Trabectedin	9	4	13 (9%)
Pazopanib	4	5	9 (6.2%)
Gemcitabine	7	0	7 (4.8%)
Axitinib	4	1	5 (3.5%)
Doxorubicin and ifosfamide	0	4	4 (2.8%)
NGR-nTNF and doxorubicin	0	3	3 (2.1%)
Caelyx™	1	0	1 (0.7%)
Anastrozole	0	1	1 (0.7%)
Dacarbazine	1	0	1 (0.7%)
Imatinib	1	0	1 (0.7%)
Paclitaxel	1	0	1 (0.7%)
Paclitaxel and hedgehog inhibitor	0	1	1 (0.7%)
Unknown	0	1	1 (0.7%)
Total	62	83	145

* Two patients were prescribed 2 drugs simultaneously; three patients were prescribed 3 drugs simultaneously

Appendix Table 11. Dose reductions per cycle

Doxorubicin dose reductions	Dose (mg/m ²)					
	50	56.25	60	63.75	75	
Cycle						
1					128 (100%)	128
2	2 (1.7%)		6 (5.1%)		110 (93.2%)	118
3	4 (4.0%)		11 (11.0%)		85 (85.0%)	100
4	4 (4.2%)		19 (20.0%)		72 (75.8%)	95
5	4 (5.1%)	1 (1.3%)	20 (25.3%)	1 (1.3%)	53 (67.1%)	79
6	3 (4.2%)		19 (26.8%)	1 (1.4%)	48 (67.6%)	71
Gemcitabine dose reductions	Dose (mg/m ²)					
	450	540	675	N		
Cycle						
1, D1			126 (100%)		126	
1, D8			118 (100%)		118	
2, D1		8 (7.3%)	102 (92.7%)		110	
2, D8		8 (7.6%)	98 (92.4%)		106	
3, D1		11 (12.4%)	78 (87.6%)		89	
3, D8		11 (12.5%)	77 (87.5%)		88	
4, D1	1 (1.3%)	12 (16.0%)	62 (82.7%)		75	
4, D8	1 (1.4%)	11 (15.5%)	59 (83.1%)		71	
5, D1	1 (1.7%)	11 (18.6%)	47 (79.7%)		59	
5, D8	1 (1.9%)	8 (15.1%)	44 (83.0%)		53	
6, D1	1 (1.9%)	9 (17.3%)	42 (80.8%)		52	
6, D8	1 (2.0%)	8 (16.3%)	40 (81.6%)		49	
Docetaxel dose reductions	Dose (mg/m ²)					
	50	60	75	N		
Cycle						
1			118 (100%)		118	
2		8 (7.6%)	98 (92.4%)		106	
3		10 (11.5%)	77 (88.5%)		87	
4	1 (1.4%)	11 (15.5%)	59 (83.1%)		71	
5	1 (1.9%)	7 (13.2%)	45 (84.9%)		53	
6	1 (2.0%)	7 (14.3%)	41 (83.7%)		49	

Appendix Table 12. Grade 3 or 4 Adverse Events associated with SNPs

Any AE grade 3 or 4 within Dox		
subgroup	Dox (N=118)	p-value
Overall	79/118(66.9%)	
CYP3A41b - AA	70/106(66.0%)	0.74
CYP3A41b - AG	8/10(80.0%)	
CYP3A41b - GG	1/2(50.0%)	
CDArS1048977 - CC	37/53(69.8%)	0.74
CDArS1048977 - CT	29/46(63.0%)	
CDArS1048977 - TT	13/19(68.4%)	
NT5C2rs11598702 - TT	26/45(57.8%)	0.16
NT5C2rs11598702 - CT	38/52(73.1%)	
NT5C2rs11598702 - CC	15/21(71.4%)	
XRCC4rs1382368 - GG	20/36(55.6%)	0.07
XRCC4rs1382368 - AG	42/60(70.0%)	
XRCC4rs1382368 - AA	17/22(77.3%)	
CYP1Brs1056836 - CC	13/19(68.4%)	0.78
CYP1Brs1056836 - CG	42/65(64.6%)	
CYP1Brs1056836 - GG	24/34(70.6%)	
SLC22A16rs12210538 - AA	45/70(64.3%)	0.7
SLC22A16rs12210538 - AG	30/41(73.2%)	
SLC22A16rs12210538 - GG	4/7(57.1%)	
CMPK1rs11211524 - AA	47/69(68.1%)	0.96
CMPK1rs11211524 - AC	30/47(63.8%)	
CMPK1rs11211524 - CC	2/2(100.0%)	
PRDX4rs518329 - GG	27/43(62.8%)	0.18
PRDX4rs518329 - AG	27/43(62.8%)	
PRDX4rs518329 - AA	25/32(78.1%)	
SLC28A3rs7867504 - TT	35/55(63.6%)	0.74
SLC28A3rs7867504 - TC	36/50(72.0%)	
SLC28A3rs7867504 - CC	8/13(61.5%)	
ABCB1rs1045642 - TT	19/28(67.9%)	0.56
ABCB1rs1045642 - CT	41/65(63.1%)	
ABCB1rs1045642 - CC	19/25(76.0%)	
NQO2rs1143684 - TT	51/70(72.9%)	0.24
NQO2rs1143684 - CT	24/43(55.8%)	
NQO2rs1143684 - CC	4/5(80.0%)	
CMPK1rs4492666 - CC	22/33(66.7%)	0.7
CMPK1rs4492666 - AC	39/60(65.0%)	
CMPK1rs4492666 - AA	18/25(72.0%)	
NQO1rs1800566 - CC	48/71(67.6%)	0.86
NQO1rs1800566 - CT	26/41(63.4%)	
NQO1rs1800566 - TT	5/6(83.3%)	
ABCB1rs1128503 - CC	29/45(64.4%)	0.34
ABCB1rs1128503 - CT	35/54(64.8%)	
ABCB1rs1128503 - TT	15/19(78.9%)	
CBR1rs9024 - GG	62/96(64.6%)	0.18
CBR1rs9024 - AG	15/20(75.0%)	
CBR1rs9024 - AA	2/2(100.0%)	
DCRrs4694362 - TT	25/44(56.8%)	0.09
DCRrs4694362 - CT	39/54(72.2%)	
DCRrs4694362 - CC	15/20(75.0%)	
GSTP1rs1695 - AA	40/58(69.0%)	0.2
GSTP1rs1695 - AG	33/46(71.7%)	
GSTP1rs1695 - GG	6/14(42.9%)	
SLC22A16rs714368 - AA	51/69(73.9%)	0.03
SLC22A16rs714368 - AG	27/45(60.0%)	
SLC22A16rs714368 - GG	1/4(25.0%)	
SLC29A1rs760370 - AA	26/39(66.7%)	0.72
SLC29A1rs760370 - AG	39/56(69.6%)	
SLC29A1rs760370 - GG	14/23(60.9%)	
SLCO1B3rs7311358 - AA	59/84(70.2%)	0.32
SLCO1B3rs7311358 - AG	15/26(57.7%)	
SLCO1B3rs7311358 - GG	5/8(62.5%)	
SLC22A16rs6907567 - AA	51/69(73.9%)	0.03
SLC22A16rs6907567 - AG	27/45(60.0%)	
SLC22A16rs6907567 - GG	1/4(25.0%)	
CBR3rs1056892 - GG	37/54(68.5%)	0.8
CBR3rs1056892 - AG	32/49(65.3%)	
CBR3rs1056892 - AA	10/15(66.7%)	
SLC29A1rs9394992 - CC	47/67(70.1%)	0.43
SLC29A1rs9394992 - CT	27/43(62.8%)	
SLC29A1rs9394992 - TT	5/8(62.5%)	
CDArS2072671 - AA	41/56(73.2%)	0.06
CDArS2072671 - AC	34/52(65.4%)	
CDArS2072671 - CC	4/10(40.0%)	
SLC22A16rs723685 - TT	69/97(71.1%)	0.04
SLC22A16rs723685 - CT	10/21(47.6%)	
SLC22A16rs723685 - CC	0/0(.%)	
RRM1rs9937 - AA	18/29(62.1%)	0.63
RRM1rs9937 - AG	44/64(68.8%)	
RRM1rs9937 - GG	17/25(68.0%)	
SLCO1B3rs11045585 - AA	59/86(68.6%)	0.88
SLCO1B3rs11045585 - AG	15/26(57.7%)	
SLCO1B3rs11045585 - GG	5/6(83.3%)	

Any AE grade 3 or 4 within GemDoc		
subgroup	GemDoc (N=121)	p-value
Overall	89/121(73.6%)	
CYP3A41b - AA	80/111(72.1%)	0.15
CYP3A41b - AG	7/8(87.5%)	
CYP3A41b - GG	2/2(100.0%)	
CDArS1048977 - CC	41/54(75.9%)	0.53
CDArS1048977 - CT	42/58(72.4%)	
CDArS1048977 - TT	6/9(66.7%)	
NT5C2rs11598702 - TT	36/46(78.3%)	0.36
NT5C2rs11598702 - CT	40/56(71.4%)	
NT5C2rs11598702 - CC	13/19(68.4%)	
XRCC4rs1382368 - GG	30/41(73.2%)	0.61
XRCC4rs1382368 - AG	44/57(77.2%)	
XRCC4rs1382368 - AA	15/23(65.2%)	
CYP1Brs1056836 - CC	24/28(85.7%)	0.32
CYP1Brs1056836 - CG	40/59(67.8%)	
CYP1Brs1056836 - GG	25/34(73.5%)	
SLC22A16rs12210538 - AA	55/75(73.3%)	0.74
SLC22A16rs12210538 - AG	30/39(76.9%)	
SLC22A16rs12210538 - GG	4/7(57.1%)	
CMPK1rs11211524 - AA	50/73(68.5%)	0.12
CMPK1rs11211524 - AC	34/42(81.0%)	
CMPK1rs11211524 - CC	5/6(83.3%)	
PRDX4rs518329 - GG	35/49(71.4%)	0.84
PRDX4rs518329 - AG	27/35(77.1%)	
PRDX4rs518329 - AA	27/37(73.0%)	
SLC28A3rs7867504 - TT	40/53(75.5%)	0.95
SLC28A3rs7867504 - TC	43/61(70.5%)	
SLC28A3rs7867504 - CC	6/7(85.7%)	
ABCB1rs1045642 - TT	22/30(73.3%)	0.96
ABCB1rs1045642 - CT	50/68(73.5%)	
ABCB1rs1045642 - CC	17/23(73.9%)	
NQO2rs1143684 - TT	50/67(74.6%)	0.89
NQO2rs1143684 - CT	32/46(69.6%)	
NQO2rs1143684 - CC	7/8(87.5%)	
CMPK1rs4492666 - CC	27/33(81.8%)	0.03
CMPK1rs4492666 - AC	46/60(76.7%)	
CMPK1rs4492666 - AA	16/28(57.1%)	
NQO1rs1800566 - CC	57/79(72.2%)	0.33
NQO1rs1800566 - CT	26/36(72.2%)	
NQO1rs1800566 - TT	6/6(100.0%)	
ABCB1rs1128503 - CC	26/36(72.2%)	0.87
ABCB1rs1128503 - CT	46/62(74.2%)	
ABCB1rs1128503 - TT	17/23(73.9%)	
CBR1rs9024 - GG	63/89(70.8%)	0.19
CBR1rs9024 - AG	24/30(80.0%)	
CBR1rs9024 - AA	2/2(100.0%)	
DCKrs4694362 - TT	32/44(72.7%)	0.57
DCKrs4694362 - CT	46/59(78.0%)	
DCKrs4694362 - CC	11/18(61.1%)	
GSTP1rs1695 - AA	41/55(74.5%)	0.99
GSTP1rs1695 - AG	35/49(71.4%)	
GSTP1rs1695 - GG	13/17(76.5%)	
SLC22A16rs714368 - AA	50/74(67.6%)	0.03
SLC22A16rs714368 - AG	34/42(81.0%)	
SLC22A16rs714368 - GG	5/5(100.0%)	
SLC29A1rs760370 - AA	41/50(82.0%)	0.11
SLC29A1rs760370 - AG	38/56(67.9%)	
SLC29A1rs760370 - GG	10/15(66.7%)	
SLCO1B3rs7311358 - AA	63/87(72.4%)	0.37
SLCO1B3rs7311358 - AG	21/29(72.4%)	
SLCO1B3rs7311358 - GG	5/5(100.0%)	
SLC22A16rs6907567 - AA	50/74(67.6%)	0.03
SLC22A16rs6907567 - AG	34/42(81.0%)	
SLC22A16rs6907567 - GG	5/5(100.0%)	
CBR3rs1056892 - GG	30/45(66.7%)	0.12
CBR3rs1056892 - AG	43/57(75.4%)	
CBR3rs1056892 - AA	16/19(84.2%)	
SLC29A1rs9394992 - CC	46/61(75.4%)	0.81
SLC29A1rs9394992 - CT	36/51(70.6%)	
SLC29A1rs9394992 - TT	7/9(77.8%)	
CDArS2072671 - AA	46/64(71.9%)	0.99
CDArS2072671 - AC	33/42(78.6%)	
CDArS2072671 - CC	10/15(66.7%)	
SLC22A16rs723685 - TT	69/98(70.4%)	0.08
SLC22A16rs723685 - CT	19/22(86.4%)	
SLC22A16rs723685 - CC	1/1(100.0%)	
RRM1rs9937 - AA	18/31(58.1%)	0.05
RRM1rs9937 - AG	47/60(78.3%)	0.05
RRM1rs9937 - GG	24/30(80.0%)	0.05
SLCO1B3rs11045585 - AA	64/88(72.7%)	0.53
SLCO1B3rs11045585 - AG	22/30(73.3%)	0.53
SLCO1B3rs11045585 - GG	3/3(100.0%)	0.53