Appendix 1. Additional clinical effectiveness results from JGDG

Table A1: Baseline characteristics of patients in phase 2 (ITT population)

Parameters	JGDG phase 2	
	OlaDox N = 66	Dox N=67
Sex, n (%)		
Female	40 (61%)	34 (51%)
Male	26 (39%)	33 (49%)
Age (years)		
Median age (range)	58.5 (22–85)	58.0 (29–86)
Race, n (%)		
White	55 (83%)	60 (90%)
Black	6 (9%)	5 (8%)
Asian	2 (3%)	2 (3%)
Native Hawaiian or other Pacific Islander	1 (2%)	0
Other	2 (3%)	0
Ethnic origin, n (%)		
Hispanic or Latino	6 (9%)	2 (3%)
Not Hispanic or Latino	60 (91%)	64 (96%)
Missing	0	1 (2%)
ECOG performance status, n (%)		
0-1	62 (94%)	63(94%)
2	4 (6%)	4 (6%)
PDGFRα status*, n (%)		
Stratification assay		
Positive	58 (88%)	59 (88%)
Negative	8 (12%)	8 (12%)
Exploratory assay (post hoc)†		
Positive	18 (33%)	19 (34%)
Negative	37 (67%)	37 (66%)
Histological type, n (%)		
Leiomyosarcoma	24 (36%)	27 (40%)
Non-leiomyosarcoma‡	42 (64%)	40 (60%)
Previous treatments, n (%) (IVRS categorisation)^^		
0	27 (41%)	31 (46%)
≥1	39 (59%)	36 (54%)
Previous treatments, n (%) (CRF)^^		
0	40 (61%)	47 (70%)
≥1	26 (39%)	20 (30%)

Histological type, n (%)		
Leiomyosarcoma	24 (36%)	27 (40%)
Undifferentiated pleomorphic sarcoma	10 (15%)	14 (21%)
Liposarcoma	8 (12%)	15 (22%)
Angiosarcoma	4 (6%)	3 (5%)
Synovial sarcoma	1 (2%)	2 (3%)
Neurofibrosarcoma	1 (2%)	0
Fibrosarcoma	1 (2%)	0
Other**	17 (26%)	6 (9%)
Alveolar soft part sarcoma	1 (1.5%)	0
Chondrosarcoma bone	0	2(3.0%)
Clear cell sarcoma	1 (1.5%)	0
Endometrial stromal sarcoma	1 (1.5%)	0
Epithelioid sarcoma	2(3.0%)	0
Extraskeletal chondrosarcoma	0	1 (1.5%)
Extraskeletal myxoid chondrosarcoma	1 (1.5%)	0
Fibromyxoid sarcoma	1 (1.5%)	1 (1.5%)
Fibrosarcomatous transformation in a recurrent dermatofibrosarcoma	1 (1.5%)	0
Hemangiopericytoma	1 (1.5%)	1 (1.5%)
Malignant glomus tumour	1 (1.5%)	0
Malignant peripheral nerve sheath tumour	1 (1.5%)	0
Malignant solitary fibrous tumour	1 (1.5%)	0
Myxofibrosarcoma	1 (1.5%)	0
Myxoid chondrosarcoma	1 (1.5%)	0
Myxoid sarcoma	0	1 (1.5%)
Soft tissue undifferentiated round cell carcinoma negative for EWS	1 (1.5%)	0
Undifferentiated neoplasm	1 (1.5%)	0
Undifferentiated uterine sarcoma	1 (1.5%)	0

Key: ECOG, Eastern Cooperative Oncology Group; PDGFRα, platelet-derived growth factor receptor.
Notes: *PDGFRα-positive status was defined as a staining result of 2+ or greater. The results from stratification assay results were used to stratify randomisation. †A positive status corresponds to weak intensity membranous staining comprising more than 30% of the tumour or moderate-to-strong intensity membranous staining comprising more than 5% of the tumour, or both. A negative status corresponds to staining that does not meet these requirements. **Other subtypes were entered into the case report form as free text fields; therefore, some histologies were consolidated. For example, epithelioid and epithelioid sarcoma were merged, and chondrosarcoma bone and chondrosarcoma primary bone were merged.^^The IVRS categorisation of patients at randomisation based on the number of previous lines of treatment appears to have been interpreted by study sites as including systemic therapies for adjuvant or neoadjuvant treatment. Analysing using CRF data instead of IVRS excludes systemic therapies for adjuvant or neoadjuvant treatment
Source: Eli Lilly submission, Section 4.5, pp54-55

Appendix 2. Adverse events

Table A2: Overview of Treatment-Emergent Adverse Events Phase 2, Safety

	OlaDox N = 64 n (%)	Dox N = 65 n (%)
Any AE	**63 (98.4)**	**64 (98.5)**
Related to any Study Drug	63 (98.4)	63 (96.9)
Related to Olaratumab	56 (87.5)	NA
Related to Doxorubicin	62 (96.9)	63 (96.9)
Any Serious Adverse Event	**27 (42.2)**	**25 (38.5)**
Related to any Study Drug	14 (21.9)	17 (26.2)
Related to Olaratumab	10 (15.6)	NA
Related to Doxorubicin	12 (18.8)	17 (26.2)
Any Grade ≥3 AE	**51 (79.7)**	**45 (69.2)**
Related to any Study Drug	43 (67.2)	36 (55.4)
Related to Olaratumab	29 (45.3)	NA
Related to Doxorubicin	40 (62.5)	36 (55.4)
Any AE Leading to Discontinuation of any Study Drug	**8 (12.5)**	**12 (18.5)**
Any AE Leading to Discontinuation of Olaratumab Only	1 (1.6)	NA
Any AE Leading to Discontinuation of Doxorubicin Only	3 (4.7)	12 (18.5)
Any AE Leading to Discontinuation of both Olaratumab and Doxorubicin	4 (6.3)	0
Any AE with Outcome of Death within 30 Days of Last Dose	**0**	**5 (7.7)[a]**
Related to any Study Drug	0	2 (3.1)
Related to Olaratumab	0	NA
Related to Doxorubicin	0	2 (3.1)

Abbreviations: AE = adverse event; N = number of treated patients; NA = not applicable. Data cut-off date: 16 May 2015.

a.Deaths are counted for both the doxorubicin treatment and during the olaratumab monotherapy stage. There were 4 deaths that occurred within 30 days of last dose of doxorubicin. There was 1 death that occurred after the patient received olaratumab monotherapy. Note: Adverse event with missing or unknown relationship to study drug is counted as 'related'.

Table A3: Summary of Treatment-Emergent Adverse Events Phase 2, Safety

	OlaDox (n=64)			Dox (n=65)		
	Any Grade	Grade 3	Grade ≥ 4	Any Grade	Grade 3	Grade ≥ 4
Patients with any adverse event †	63 (98%)	24 (38%)	27 (42%)	64 (98%)	25 (38%)	20 (31%)
Nausea	47 (73%)	1 (2%)	0	34 (52%)	2 (3%)	0
Fatigue ‡	44 (69%)	6 (9%)	0	45 (69%)	2 (3%)	0
Neutropenia§¶	37 (58%)	12 (19%)	22 (34%)	23 (35%)	5 (8%)	16 (25%)
Mucositis||	34 (53%)	2 (3%)	0	23 (35%)	3 (5%)	0
Alopecia	33 (52%)	0	0	26 (40%)	0	0

Vomiting	29 (45%)	0	0	12 (18%)	0	0
Anaemia**	26 (41%)	8 (13%)	0	24 (37%)	6 (9%)	0
Leucopoenia † † ¶	26 (41%)	14 (22%)	9 (14%)	12 (18%)	5 (8%)	6 (9%)
Constipation	22 (34%)	0	0	21 (32%)	1 (2%)	0
Diarrhoea	22 (34%)	2 (3%)	0	15 (23%)	0	0
Decreased appetite	20 (31%)	1 (2%)	0	13 (20%)	0	0
Abdominal pain ‡ ‡	15 (23%)	2 (3%)	0	9 (14%)	0	0
Pyrexia	15 (23%)	0	0	12 (18%)	0	0
Musculoskeletal pain§§	41 (64%)	¶¶	¶¶	16 (25%)	||||	||||
Febrile neutropenia***	8 (13%)	7 (11%)	1 (1.6%)	9 (14%)	9 (14%)	0
Infections and infestations*** † † †	27 (42%)	5 (8%)	0	27 (42%)	4 (6%)	3 (5%)
Infusion-related reaction*** ‡ ‡ ‡	8 (13%)	0	2 (3%)	0	0	0
Treatment-related adverse event	63 (98%)	18 (28%)	25 (39%)	63 (97%)	19 (29%)	17 (26%)
Adverse event leading to discontinuation of treatment	8 (13%)	1 (2%)	3 (5%)	12 (18%)	3 (5%)	5 (8%)
Serious adverse event						
Any event	27 (42%)	20 (31%)	7 (11%)	25 (38%)	14 (22%)	8 (12%)
Treatment-related event	14 (22%)	8 (13%)	6 (9%)	17 (26%)	11 (17%)	5 (8%)
Cardiac dysfunction§§§¶¶¶	15 (23%)	1 (2%)	0	11 (17%)	0	0
Oedema peripheral	10 (16%)	0	0	7 (11%)	0	0
Ejection fraction decreased	5 (8%)	1 (2%)	0	4 (6%)	0	0
Congestive cardiac failure	1 (2%)	1 (2%)	0	0	0	0
Hepatojugular reflux	1 (2%)	0	0	0	0	0
Jugular vein distension	1 (2%)	0	0	0	0	0
Left ventricular dysfunction	1 (2%)	0	0	0	0	0
Cardiac dysfunction (excluding peripheral oedema) ||||||	5 (8%)	1 (2%)	0	4 (6%)	0	0
LVEF (lowest post-baseline)						
n****	51	..	..	32	..	..
LVEF <50%	6 (12%)	..	..	3 (9%)	..	..

Data are n (%). LVEF=left ventricular ejection fraction. *Adverse events and clinical laboratory toxicity were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0). †The adverse events listed here were reported in at least 15% of patients in the olaratumab plus doxorubicin group, except as noted in footnote ¶¶. These included individual preferred terms from the Medical Dictionary for Regulatory Activities (MedDRA) and specific c consolidated terms combining clinically synonymous MedDRA preferred terms. ‡Consolidated term comprising the following preferred terms: fatigue and asthenia. §Consolidated term comprising the following preferred terms: neutropenia and neutrophil count decreased. ¶Some patients reported both neutropenia and leukopenia. ||Consolidated term comprising the following preferred terms: mucosal inflammation, oropharyngeal pain, and stomatitis.**Consolidated term comprising the following preferred terms: anaemia and haemoglobin decreased. ††Consolidated term comprising the following preferred terms: leukopenia and white blood cell count decreased. ‡‡Consolidated term comprising the following preferred terms: abdominal pain upper, abdominal pain, and abdominal pain lower. §§Preferred terms reported were: arthralgia, back pain, spasms, musculoskeletal chest pain, myalgia, and pain in extremity. ¶¶5 (7.8%) patients (%) had musculoskeletal pain of grade ≥3 in the olaratumab plus doxorubicin group. |||| 1 (1.5%) patient had musculoskeletal pain of grade ≥3 in the doxorubicin group. ***These events are included here because they were considered clinically important.†††Includes all preferred terms within the MedDRA system organ class of infections and infestations. ‡‡‡Consolidated term comprising the following preferred terms (from AESI): hypersensitivity, infusion-related reaction, and face oedema. §§§Includes individual preferred terms from

MedDRA. ¶¶¶Some patients reported more than one cardiac dysfunction event term. ||||||No patients with reported adverse events of peripheral oedema had any reported adverse events to suggest cardiac dysfunction.****Number of patients assessed at baseline and at least one post-baseline time point.

Appendix 3. Populations in network meta-analysis

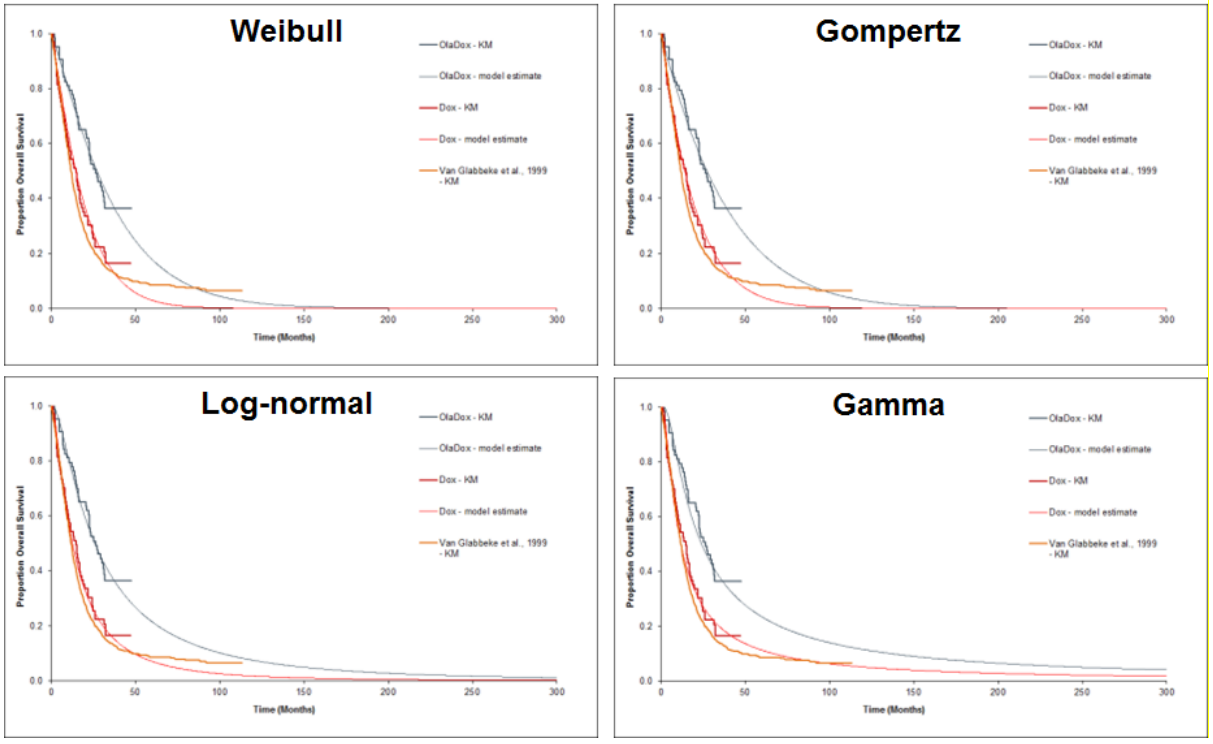
Table A4: Baseline charatceristics of populations includes in the network meta-analysis

	Tap		Seddon		Judson		Le Cesne		Santaro		Maurel	
	OlaDox (n=66)	Dox (n=67)	GemDoc (n=128)	Dox (n=129)	IfoDox (n=227)	Dox (n=228)	IfoDox (n=157)	IfoDox + [a]rhGM-CSF (n=157)	IfoDox (n=258)	Dox (n=263)	IfoDox (n=65)	Dox (n=67)
Age												
Median (range)	58.5 (22-85)	58.0 (29-86)	55 (21-75)	56 (19-82)	47 (18-63)	48 (18-60)	50 (19-74)	50 (20-76)	50	52	50 (18-65)	49 (18-68)
Sex												
Men (%)	26 (39)	33 (49)	51 (40)	50 (39)	114 (50)	103 (45)	60	64	129 (50)	125 (48)	36 (55)	41 (61)
Women	40 (61)	34 (51)	77 (60)	79 (61)	113 (50)	125 (55)	89	81	129 (50)	138 (53)	29 (45)	26 (39)
Race												
White	55 (83)	60 (90)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Black	6 (9)	5 (8)										
Asian	2 (3)	2 (3)										
Other	3 (5)	0										
ECOG												
0-1	62 (94)	63 (94)	NR	NR	NR	NR	NR	NR	212 (82)	218 (83)	65 (100)	67 (100)
2	4 (6)	4 (6)							45 (17)	45 (17)		
Histological type												
Leiomyosarcoma	24 (36)	27 (40)	[b]35 (27)	[b]36 (28)	59 (26)	54 (24)	53	59	NR	NR	20 (31)	15 (22)
Non-Leiomyosarcoma	42 (64)	40 (60)	93 (74)	93 (72)	168 (74)	174 (76)	95	86			66 (78)	52 (69)
Previous treatments												
0	27 (41)	31 (46)	128	129	[c]Unclear	[c]Unclear	157	157	258	263	65	67
≥1	39 (59)	36 (54)	0	0			0	0	0	0	0	0
WHO PS												
0 (%)	NR	NR	52 (41)	55 (43)	123 (54)	129 (57)	NR	NR	NR	NR	NR	NR
1 (%)			67 (52)	63 (49)	103 (45)	98 (43)						
2 (%)			9 (7)	11 (9)	1 (<1%)	1 (<1)						
Karnofsky PS												
100-90	NR	NR	NR	NR	NR	NR	103	102	NR	NR	NR	NR
80-70							46	43				

Key: a, recombinant human granulocyte-macrophage colony-stimulating factor; b,Uterine leiomyosarcoma; c, Previous adjuvant chemotherapy allowed if disease progression had not occurred within six months of completion; NR, not reported

Appendix 4. Comparison of ITT OS data from JGDG trial with external data

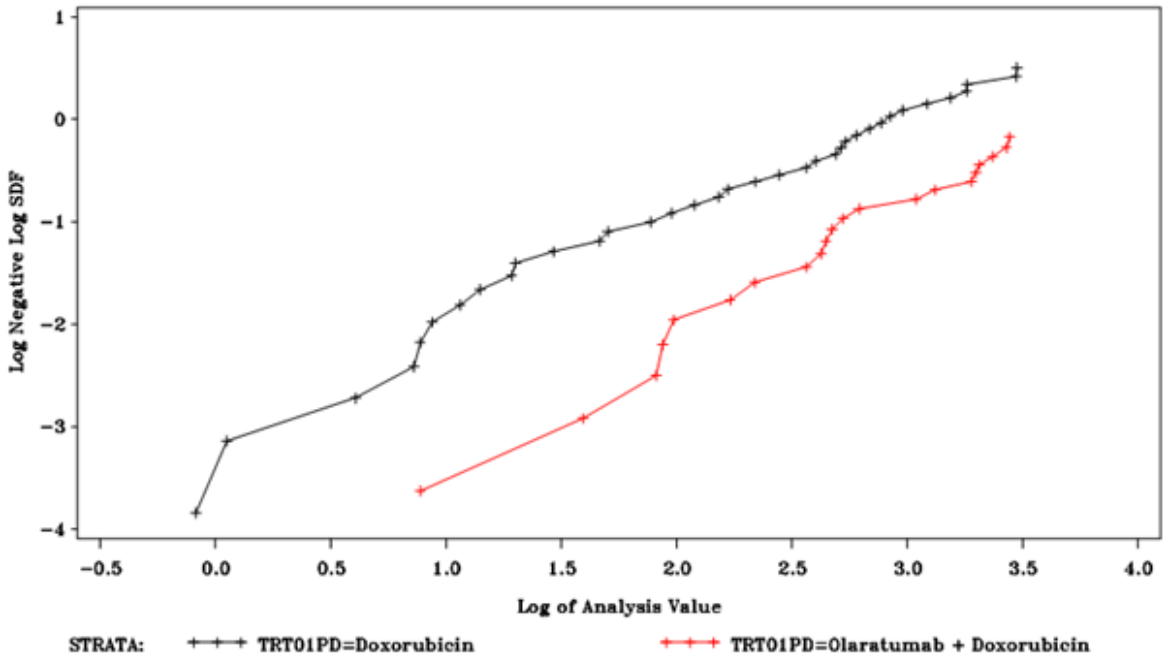
Figure A1: Comparison of ITT OS parametric survival models "arms together functions" with Van Glabbeke study results



Source: Eli Lilly submission, figure 33, p. 149.

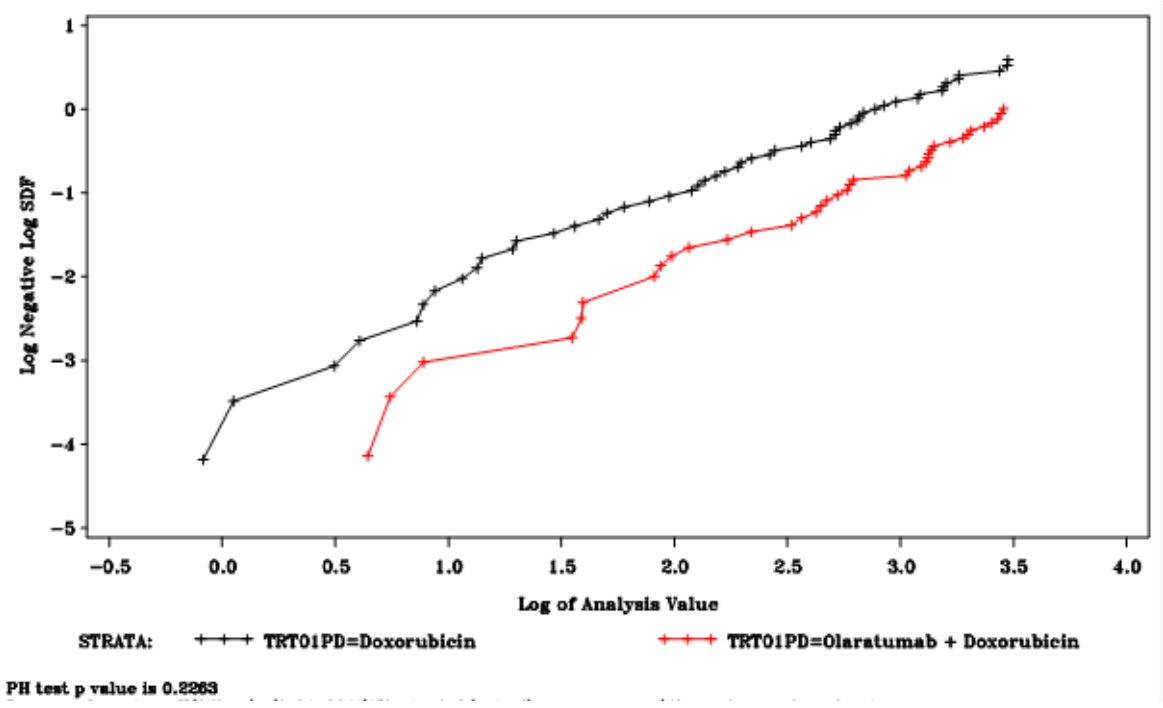
Appendix 5. Log cumulative hazard plots of OS

Figure A2. OS Log cumulative hazard plot (first-line population)



Source: Lilly's submission, Fig. 27, p. 142

Figure A3. OS Log cumulative hazard plot (ITT population)



Source: Lilly's submission, Fig. 28, p. 142

Appendix 6. Adverse event costs and utility decrements

Table A5. Summary of Base-Case Grade ≥ 3 Adverse-Event Costs and Utility Decrements Applied in the Economic Model

Grade ≥ 3 Adverse Event	Utility Decrement		Duration (Weeks)[a] OlaDox		Duration (Weeks)[a] Dox		Source for the Utility Decrement
	Mean	SE[b]	Mean	SE[c]	Mean	SE[c]	
Anaemia	0.119	0.023	5.7	0.57	5.7	0.57	(4)(referenced to (5)
Back pain	0.236	0.028	0.6	0.06	0.6	0.06	(6)
Congestive heart failure	0.200	0.020	3.0	0.30	3.0	0.30	(4)[d]
Diarrhoea	0.327	0.025	1.0	0.10	1.0	0.10	(6)
Dyspnoea	0.242	0.025	1.0	0.10	1.0	0.10	(6)
Fatigue	0.262	0.025	0.6	0.06	0.6	0.06	(6)
Febrile neutropenia	0.090	0.016	0.8	0.08	0.8	0.08	(4) (referenced to (7)
GI perforation	0.118	0.012	0.1	0.01	0.1	0.01	Assumption: same as anaemia
Grade 4 neutropenia without fever/infection	0.090	0.015	1.4	0.14	1.4	0.14	(4) (referenced to (7)
Hepatic toxicity	0.000	—	1.0	0.1	1.0	0.1	(4))[e]
Infection	0.090	0.016	1.3	0.13	1.3	0.13	Assumption: same as febrile neutropenia
Mucositis	0.151	0.015	0.9	0.10	0.9	0.10	(8)
Nausea/vomiting	0.357	0.024	0.7	0.10	0.7	0.10	(6)
Pain in extremity	0.236	0.028	0.7	0.07	0.7	0.07	(6)
Thrombocytopenia	0.090	0.016	0.1	0.01	0.1	0.01	Assumption from (6) same as neutropenia
Venous thromboembolism	0.050	0.012	0.5	0.10	0.5	0.10	(2008 (9))

ALT = alanine transaminase; AST = aspartate transaminase; CHF = congestive heart failure; Dox = Doxorubicin; GI = gastrointestinal; IfoDox = ifosfamide + Doxorubicin; NE = cannot be estimated; SE = standard error.
a JGDG data reviewed and adjusted based on expert opinion (UK Advisory Board Meeting, 12th April 2016)
b Beta distribution.
c Measure of uncertainty assumed to be 10% of the mean.
d Reported as an assumption (cardiac toxicity/left ventricular dysfunction).
e Reported as an assumption (ALT/AST elevation).
Source: Eli Lilly submission, table 56, p. 175

Table A6: Summary of Base-Case Grade 1-2 Adverse-Event Costs and Utility Decrements Applied in the Economic Model

Grade 1-2 Adverse Event	Utility Decrement		Duration (Weeks)[a]				Source for the Utility Decrement
			OlaDox		Dox		
	Mean	SE	Mean	SE[b]	Mean	SE[b]	
Diarrhea	0.060	0.010	1.5	0.150	1.5	0.150	Beusterien et al. (2009) (flu-like syndrome)
Fatigue	0.090	0.010	3.3	0.330	3.3	0.330	Beusterien et al. (2009)
Mucositis	0.100	0.020	3.1	0.310	3.1	0.310	Beusterien et al. (2009) (stomatitis)
Nausea	0.070	0.010	3.0	0.300	3.0	0.300	Beusterien et al. (2009)
Vomiting	0.070	0.010	1.5	0.150	1.5	0.150	Beusterien et al. (2009)

Dox = Doxorubicin; OlaDox = olaratumab + Doxorubicin; SE = standard error;
a JGDG validated by input from advisors at the UK Advisory Board Meeting on April 12, 2016. Values for which JGDG data were not available are based on advisor feedback alone.
b Measure of uncertainty assumed to be 10% of the mean.
Source: Eli Lilly submission, table 57, p. 176

Table A7: Unit costs of grade 3/4 adverse events in the model

Grade ≥ 3 adverse events	Cost	Source / Comment
Anaemia	£1,063	NHS Reference Costs 2014-15 (10) SA04G-SA04L Iron deficiency anaemia with CC Elective Inpatients (EI), weighted average
Back pain	£1,500	NHS Reference Costs 2014-15 (10) HC32H-HC32K Low back pain with CC; Elective weighted average
Congestive Heart Failure	£2,783	NHS Reference Costs 2014-15 (10) EB03A- EB03E Heart failure or shock with CC; Elective inpatients and non-Elective long stay, weighted average
Diarrhoea	£1,311	NHS Reference Costs 2014-15 (10) FZ91A- FZ91M Non-Malignant Gastrointestinal Tract Disorders with Multiple Interventions, with CC; non-Elective Long stay / short stay, weighted average
Dyspnoea	£405	NHS Reference Costs 2014-15 (10) DZ19L- DZ19N Other Respiratory Disorders without Interventions, with CC; non-Elective short stay, weighted average
Fatigue	£388	NHS Reference Costs 2014-15 (10) (EB03A- EB03E) Soft Tissue Disorders with CC; non-Elective Long Stay ,weighted average
Febrile neutropenia	£3,529	NHS Reference Costs 2012-13; (inflated to 2014-15 costs) (10) PA45Z, Febrile Neutropenia with Malignancy;
GI perforation	£1,583	NHS Reference Costs 2014-15 (10) FZ38M- FZ38P Gastrointestinal Bleed without Interventions, with CC Score; Non-Elective Long stay , weighted average
Grade 4 neutropenia w/o fever / infection	£167	NHS Reference costs, 2014-15; (10)

		WF01A - consultant led, Service Code 370/ BNF 69 (March-Sep 2015), Non-Admitted Face to Face Attendance, Follow-up;
Hepatic toxicity	£2,261	NHS Reference Costs 2014-15 (10) GC01E- GC01F, Long Stay, Liver Failure Disorders without Interventions, with CC; weighted average
Infection	£3,532	NHS Reference Costs 2012-13 (10) PA45Z, Febrile Neutropenia with Malignancy; (Assumption same as febrile neutropenia)
Mucositis	£!,663	NHS Reference Costs 2014-15 (10) FZ36M- FZ36Q, Gastrointestinal Infections without Interventions, with CC; EIective, weighted average
Nausea/vomiting	£825	NHS Reference Costs 2014-15 (10) FZ13C, Minor Therapeutic or Diagnostic, General Abdominal Procedures, 19 years and over; non-Elective short stay
Pain in extremity	£1,500	NHS Reference Costs 2014-15 HC32H-J-K) Low back pain with CC; Elective; weighted average (10) Assumption: same as back pain
Thrombocytopenia	£1,453	NHS Reference Costs 2014-15 (10) SA12G- SA12K, Thrombocytopenia with CC; Short/Long stay, weighted average
Venous thromboembolism	£974	NHS Reference Costs 2014-15 (10) YQ51A- YQ51E), Deep Vein Thrombosis with CC; Short/Long stay , weighted average

Source: Eli Lilly submission, table 66, pp. 187-188

Table A8: Resource use and grade 3/4 adverse event costs in the model (base case analysis)

Grade 3/4 Adverse Event	n/N (%) Events Requiring Hospitalisation[a]	% Events requiring hospitalisation (clinical opinion)	Unit Cost per Hospitalisation[b]	Cost in model
Anemia	1/21 (5%)	5%	£1,063	£492
Back pain	4/4 (100%)	100%	£1,500	£1,667
Congestive heart failure	0/0 (100%)	100%	£2,783	£ 2,951
Diarrhea	0/2 (0%)	100%	£1,311	£1,478
Dyspnea	1/2 (50%)	50%	£405	£ 370
Fatigue	1/12 (8%)	8%	£388	£199
Febrile neutropenia	17/18 (94%)	100%	£3,529	£3,699
GI perforation	1/1 (100%)	100%	£1,583	£1,750
Grade 4 neutropenia without fever/infection	3/41 (7%)	0%	£167	£167
Hepatic hemorrhage	1/1 (100%)	100%	£2,261	£2,428
Infection	14/15 (93%)	93%	£3,532	£3,464
Mucositis	0/0 (NE)	100%	£1,663	£1,830
Nausea/vomiting	0/4 (0%)	100%	£825	£992
Pain in extremity	3/4 (75%)	75%	£1,500	£1,292
Thrombocyto-penia	2/22 (9%)	9%	£1,453	£299
Venous thromboembolism	0/0 (NE)	100%	£974	£1,141

NE = cannot be estimated; Note: the table shows the derivation of the cost per hospitalisation. The total cost of each adverse event (presented in Table 23) was calculated by multiplying this cost and the percentage of patients hospitalised (shown in column 2) and adding the cost of a specialist visit. For grade 3/4 anaemia, the cost of a blood transfusion (2 units) was added. For grade 3/4 febrile neutropenia the cost of granulocyte colony-stimulating factor for all treatment cycles was added.
[a] Data from Study JGDG, both treatment arms combined.
[b] NHS reference cost; weighted average of relevant HRG codes.
Source: Eli Lilly submission, table 67, pp. 189

Table A9: Summary of Base-Case Grade 1-2 Adverse-Event Costs and Utility Decrements Applied in the Economic Model

Grade 1-2 Adverse Event	Utility Decrement		Duration (Weeks)a				Source for the Utility Decrement
			OlaDox		Dox		
	Mean	SE	Mean	SEb	Mean	SEb	
Diarrhea	0.060	0.010	1.5	0.150	1.5	0.150	Beusterien et al. (2009) (flu-like syndrome)
Fatigue	0.090	0.010	3.3	0.330	3.3	0.330	Beusterien et al. (2009)
Mucositis	0.100	0.020	3.1	0.310	3.1	0.310	Beusterien et al. (2009) (stomatitis)
Nausea	0.070	0.010	3.0	0.300	3.0	0.300	Beusterien et al. (2009)
Vomiting	0.070	0.010	1.5	0.150	1.5	0.150	Beusterien et al. (2009)

Dox = Doxorubicin; OlaDox = olaratumab + Doxorubicin; SE = standard error;

a JGDG validated by input from advisors at the UK Advisory Board Meeting on April 12, 2016. Values for which JGDG data were not available are based on advisor feedback alone.

b Measure of uncertainty assumed to be 10% of the mean.

Tables 28 29 source: Eli Lilly submission, table 56-57, pp. 167-168.

Table A10. Unit costs of grade 3/4 adverse events in the model

Grade ≥ 3 adverse events	Cost	Source / Comment
Anaemia	£1,063	NHS Reference Costs 2014-15 (10) SA04G-SA04L Iron deficiency anaemia with CC Elective Inpatients (EI), weighted average
Back pain	£1,500	NHS Reference Costs 2014-15 (10) HC32H-HC32K Low back pain with CC; Elective weighted average
Congestive Heart Failure	£2,783	NHS Reference Costs 2014-15 (10) EB03A- EB03E Heart failure or shock with CC; Elective inpatients and non-Elective long stay, weighted average
Diarrhoea	£1,311	NHS Reference Costs 2014-15 (10) FZ91A- FZ91M Non-Malignant Gastrointestinal Tract Disorders with Multiple Interventions, with CC; non-Elective Long stay / short stay, weighted average
Dyspnoea	£405	NHS Reference Costs 2014-15 (10) DZ19L- DZ19N Other Respiratory Disorders without Interventions, with CC; non-Elective short stay, weighted average
Fatigue	£388	NHS Reference Costs 2014-15 (10) (EB03A- EB03E) Soft Tissue Disorders with CC; non-Elective Long Stay ,weighted average
Febrile neutropenia	£3,529	NHS Reference Costs 2012-13; (inflated to 2014-15 costs) (10)

		PA45Z, Febrile Neutropenia with Malignancy;
GI perforation	£1,583	NHS Reference Costs 2014-15 (10) FZ38M- FZ38P Gastrointestinal Bleed without Interventions, with CC Score; Non-Elective Long stay , weighted average
Grade 4 neutropenia w/o fever / infection	£167	NHS Reference costs, 2014-15; (10) WF01A - consultant led, Service Code 370/ BNF 69 (March-Sep 2015), Non-Admitted Face to Face Attendance, Follow-up;
Hepatic toxicity	£2,261	NHS Reference Costs 2014-15 (10) GC01E- GC01F, Long Stay, Liver Failure Disorders without Interventions, with CC; weighted average
Infection	£3,532	NHS Reference Costs 2012-13 (10) PA45Z, Febrile Neutropenia with Malignancy; (Assumption same as febrile neutropenia)
Mucositis	£!,663	NHS Reference Costs 2014-15 (10) FZ36M- FZ36Q, Gastrointestinal Infections without Interventions, with CC; Elective, weighted average
Nausea/vomiting	£825	NHS Reference Costs 2014-15 (10) FZ13C, Minor Therapeutic or Diagnostic, General Abdominal Procedures, 19 years and over; non-Elective short stay
Pain in extremity	£1,500	NHS Reference Costs 2014-15 HC32H-J-K) Low back pain with CC; Elective; weighted average (10) Assumption: same as back pain
Thrombocytopenia	£1,453	NHS Reference Costs 2014-15 (10) SA12G- SA12K, Thrombocytopenia with CC; Short/Long stay, weighted average
Venous thromboembolism	£974	NHS Reference Costs 2014-15 (10) YQ51A- YQ51E), Deep Vein Thrombosis with CC; Short/Long stay , weighted average

Table A11. Resource use and grade 3/4 adverse event costs in the model (base case analysis)

Grade 3/4 Adverse Event	n/N (%) Events Requiring Hospitalisationa	% Events requiring hospitalisation (clinical opinion)	Unit Cost per Hospitalisationb	Cost in model
Anemia	1/21 (5%)	5%	£1,063	£492
Back pain	4/4 (100%)	100%	£1,500	£1,667
Congestive heart failure	0/0 (100%)	100%	£2,783	£ 2,951
Diarrhea	0/2 (0%)	100%	£1,311	£1,478
Dyspnea	1/2 (50%)	50%	£405	£ 370
Fatigue	1/12 (8%)	8%	£388	£199
Febrile neutropenia	17/18 (94%)	100%	£3,529	£3,699
GI perforation	1/1 (100%)	100%	£1,583	£1,750
Grade 4 neutropenia without fever/infection	3/41 (7%)	0%	£167	£167
Hepatic hemorrhage	1/1 (100%)	100%	£2,261	£2,428
Infection	14/15 (93%)	93%	£3,532	£3,464
Mucositis	0/0 (NE)	100%	£1,663	£1,830
Nausea/vomiting	0/4 (0%)	100%	£825	£992
Pain in extremity	3/4 (75%)	75%	£1,500	£1,292
Thrombocyto-penia	2/22 (9%)	9%	£1,453	£299
Venous thromboembolism	0/0 (NE)	100%	£974	£1,141

NE = cannot be estimated; Note: the table shows the derivation of the cost per hospitalisation. The total cost of each adverse event (presented in Table 23) was calculated by multiplying this cost and the percentage of patients hospitalised (shown in column 2) and adding the cost of a specialist visit. For grade 3/4 anaemia, the cost of a blood transfusion (2 units) was added. For grade 3/4 febrile neutropenia the cost of granulocyte colony-stimulating factor for all treatment cycles was added.

[a] Data from Study JGDG, both treatment arms combined.

[b] NHS reference cost; weighted average of relevant HRG codes.

Tables 29 and 30 source: Eli Lilly submission, tables 66-67, pp. 178-180.

Appendix 7. Base-case model inputs

Table A12: Summary of base case model inputs

Variable	Value	Measurement of Uncertainty (Distribution)	Reference
Line of therapy	first-line	N/A	
Discount rate: costs and outcomes	3.5%	N/A	NICE (2013),
Patient characteristics			
Mean age (years)	58	SE = 5.8 (normal)	Cancer Research UK (2015)
Percentage female	56%	n/N = 74/133 (beta)	Tap et al. (2016) (11)
Mean BSA (m^2)	1.91	SE = 0.191 (normal)	Health Survey for England (2013)
Mean weight (kg)	77.3	SE = 0.011 (normal)	Seddon et al. (2015) (12)
Progression-free survival (investigator assessed)			
OlaDox vs. Dox	Kaplan-Meier	SE (normal)	JGDG study
OlaDox vs. IfoDox	Fractional polynomial	Bayesian posterior distribution	NMA, Lilly data on file 1(13)
Overall survival			
OlaDox vs Dox			
OlaDox vs. Dox to last mortality event in OlaDox arm of JGDG trial (32 months)	Gamma, arms together	Variance-covariance matrix (Cholesky decomposition)	JGDG study, Lilly data on file 13(14)
Treatment effect after trial follow-up	1.00	Fixed	Assumption
Age-specific mortality rate	UK general population mortality rates by age and sex	N/A[a]	Office of National Statistics, 2014 (15)
Age-specific mortality, HR for STS vs. general population	5.19	SE = 0.519[b] (normal)	Calculated
OlaDox vs IfoDox			
OlaDox vs. IfoDox	Fractional polynomial function	Bayesian posterior distribution	NMA, Lilly data on file 1(13)
Health State Utility values			
Progression-free	0.720	SE = 0.075 (beta)	(16)
Progressed	0.560	SE = 0.051 (beta)	(16)
Drug costs (pack price)			
Ola, 190-mg vial	[redacted]	Fixed	Lilly
Ola, 500-mg vial	£1,000	Fixed	
Dox (2mg/ml), 10mg vial	£1.65	Fixed	eMIT (12 year period to end June 2015)
Dox (2mg/ml), 50mg vial	£4.16	Fixed	
Dox (2mg/ml), 200mg vial	£16.89	Fixed	
Dex, 500mg	£156.57	Fixed	

Ifo, (1mg/ml), 1000mg	£91.32	Fixed	BNF 70 (Sept 2015 - March 2016)
Ifo, (1mg/ml), 2000mg	£179.88	Fixed	
Mesna (1g/10ml), 1000mg vial	£29.41	Fixed	
Mesna (400mg/4ml), 400mg vial	£13.41	Fixed	
G-CSF (0.12mg/0.2ml), 0.12mg	£36	Fixed	
G-CSF (0.3mg/0.5 ml), 0.3mg	£58	Fixed	
G-CSF (0.48mg /0.5 ml), 0.48	£93	Fixed	
Mean dose (first-line analysis)			
OlaDox vs Dox, OlaDox arm			
Ola (mg/kg)	[redacted]	SE = 0.034 (normal)	JGDG study, Lilly data on file 4, 2016(17)
Dox (mg/m^2)	74.52	SE = 0.491 (normal)	JGDG study, Lilly data on file 4, 2016, (17)
Dex (mg/m^2) (mean among patients receiving Dex)	730.59	SE=6.860 (normal)	JGDG study, Lilly data on file 5, 2016, (18)
Percentage receiving Dex	62%	N/A (beta)	
Dox arm			
Dox (mg/m^2)	74.46	SE = 0.348	JGDG study, Lilly data on file 4, 2016, (17)
Dex (mg/m^2) (mean among patients receiving Dex)	724.43	SE=8.826 (normal)	JGDG study, Lilly data on file 5, 2016, (18)
Percentage receiving Dex	39%	N/A (beta)	JGDG study, Lilly data on file 5
Ifo (mg/m^2)	3000	SE = 300[b] (normal)	Clinical opinion
Dox (mg/m^2)	60	SE = 6[b] (normal)	Clinical opinion
Mesna (mg/m^2)	4000	SE = 400[b] (normal)	(19)
Filgrastim (mg/Kg)	0.005	SE = 0.0005[b] (normal)	(20)
Mean number of administrations (first-line analysis)			
Ola	[redacted]	SE = 3.025 (normal)	JGDG study, Lilly data on file 6, 2016, (21)
Dox	5.62	SE = 0.410 (normal)	JGDG study, Lilly data on file 6, 2016,(21)
Dex (mean among patients receiving Dex)	3.46	SE = 0.208 (normal)	JGDG Lilly data on file 7
Dox	4.22	SE = 0.382 (normal)	JGDG study, Lilly data on file 6, 2016, (21)
Dex (mean among patients receiving Dex)	3.17	SE = 0.208	JGDG study, Lilly data on file 7, 2016, (22)
Ifo	13.26	SE = 1.326[b] (normal)	(19)[d]
Dox	4.42	SE = 0.442[b] (normal)	(19)[d]
Mesna	13.26	SE = 1.326[b] (normal)	(19)[d]
Filgrastim	30.93	SE = 3.093[b] (normal)	(20)[d]
Drug administration costs			
Ola + Dox, day 1	£329.32	SE = 0.395[e] (normal)	SB13Z (Daycase); (10)
Ola + Dox + Dex, day 1	£329.32	SE = 0.395[e] (normal)	SB13Z (Daycase); (10)
Ola, day 1	£185.53	SE = 0.252[e] (normal)	SB12Z (outpatient); (10)

Ola, day 8	£204.47	SE = 0.479[e] (normal)	SB15Z (outpatient); (10)
Dox, day 1	£185.53	SE = 0.252[e] (normal)	SB12Z (outpatient); (10)
Dox + Dex, Day 1	£185.53	SE = 0.252[e] (normal)	SB12Z (outpatient); (10)
IfoDox, per cycle	£1,781.86[f]	SE[g] (normal)	DZ17V (EI); (10)
Cardiac monitoring resource use			
Percentage of patients receiving cardiac monitoring	100%	SE = 10%[b] (normal, truncated at 1)	Assumption
Cardiac monitoring unit costs			
MUGA	£192.12	SE[h] (normal)	Weighted average RN22Z; (10)
Echocardiography	£152.80	SE = 0.070[h] (normal)	EY51Z; (10)
Resource use for regular follow-up visits and imaging			
Outpatient visit and physical examination	100%	Fixed	Assumption
Computerised tomography scan	92%	n/N = 183/199 (beta)	JGDG study, Lilly data on file 9, 2016, (23)
Positron emission tomography	9%	n/N = 18/199 (beta)	JGDG study, Lilly data on file 9, 2016, (23)
Magnetic resonance imaging	14%	n/N = 27/199 (beta)	JGDG study, Lilly data on file 9, 2016, (23)
Frequency of follow-up visits and imaging (number of months between each visit)			
0-5 years	3	SE = 0.3[b] (normal)	Assumption based on clinical opinion
5-7 years	6	SE = 0.6[b] (normal)	
After 7 years	12	SE = 1.2[b] (normal)	
Regular follow-up visits and imaging, unit costs			
Outpatient visit and physical examination	£146.72	SE[i] (normal)	Weighted average WF01A; (10)
Computerised tomography scan	£120.92	SE[j] (normal)	Weighted average RD24Z; (10)
Positron emission tomography	£517.00	SE[h] (normal)	Weighted average RN07A; (10)
Magnetic resonance imaging	£124.53	SE[i] (normal)	Weighted average RD26Z; (10)
Health State Costs			
Progression-free	£131	SE – 24.2 (gamma)	UK observational study, Lilly data on file (2016f)(24)
Progressed (excluding radiotherapy/surgery costs)	£35	SE = 6.2 (gamma)	UK observational study, Lilly data on file (2016f)(24)
Post-progression treatment costs			
OlaDox, Dox, IfoDox cohorts			
Total drug cost (£)	£6,082	See footnote[k]	UK observational study, Lilly data on file, 2016, (25)
Total administration cost (£)	£1,615	See footnote[k]	UK observational study, Lilly data on file, 2016,(25)
Total AE costs (£)	£278	See footnote[k]	UK observational study, Lilly data on file,2016, (25)

AE = adverse event; BSA = body surface area; CR = complete response; Dex = dexrazoxane; Doc = docetaxel; Dox = Doxorubicin; EI = elective inpatient; HR = hazard ratio; HSCIC = Health and Social Care Information Centre; Ifo = ifosfamide; IfoDox = ifosfamide + Doxorubicin; MUGA = multigated acquisition scan; N/A = not applicable; NHS = National Health Service; NHSRC = NHS Reference Costs, 2014-2015; NICE = National Institute for Health and Care Excellence; NMA = network meta-analysis; Ola = olaratumab; OlaDox = olaratumab + Doxorubicin; OS = overall survival; PFS = progression-free survival; PR = partial response; PSA = probabilistic sensitivity analysis; SE = standard error; STS = soft tissue sarcoma; UK = United Kingdom.

a Mortality rates by age and sex are not sampled in the PSA because the rates were for the general population.
b Assumed to be 10% of the mean value
c Used in sensitivity analysis only.
d Estimated from early discontinuation and PFS data.
e The SE was derived from the interquartile range.
f Assumes 3 days of inpatient stay.
g The uncertainty (SE) is calculated separately for the cost per day of inpatient stay.
h The uncertainty (SE) is calculated for each service code used for the weighted average (NMDA, NMOP, NMOTH).
i The uncertainty (SE) is calculated for each service code used for the weighted average (370 and 800).
j The uncertainty (SE) is calculated for each service code used for the weighted average (IMAGDA, IMAGOP, IMAGOTH).
k The uncertainty is included in the total cost for all patients in the observational study. This cost is then multiplied by the probability of receiving subsequent active therapy according to the observational study.
Source: Eli Lilly submission, table 69, pp. 191-194.

Appendix 8. Sensitivity analyses

Table A13. Deterministic sensitivity analysis - OlaDox vs Dox first-line population at list price

Parameter	Value or assumption in base case	Incr. cost (£)	Incr. benefit (QALY)	ICER (£)
	Base case	[redacted]	0.89	[redacted]
Costs				
Only 500mg vial, no 190mg vial size	Includes 500mg and 190mg vial sizes	[redacted]	0.89	[redacted]
Wastage excluded (assumes vial sharing)	Wastage included	[redacted]	0.89	[redacted]
Exclude dexrazoxane costs	Includes dexrazoxane costs	[redacted]	0.89	[redacted]
OlaDox delivery cost, day 1– Lower quartile £212	Daycase £329	[redacted]	0.89	[redacted]
OlaDox delivery cost , day 1– Upper quartile £400	Daycase £329	[redacted]	0.89	[redacted]
Ola monotherapy day 1– Outpatient lower quartile £119	Daycase £186	[redacted]	0.89	[redacted]
Ola monotherapy day 1– Outpatient upper quartile £203	Daycase £186	[redacted]	0.89	[redacted]
Ola monotherapy day 8– Outpatient lower quartile £107	Outpatient £204	[redacted]	0.89	[redacted]
Ola monotherapy day 8– Outpatient upper quartile £237	Outpatient £204	[redacted]	0.89	[redacted]
Cardiac monitoring costs - Echo Lower Quartile £119	£153	[redacted]	0.89	[redacted]
Cardiac monitoring costs –Echo Upper quartile £180	£153	[redacted]	0.89	[redacted]
Cardiac monitoring costs – MUGA Upper and Lower quartile £94	£192	[redacted]	0.89	[redacted]
Source of post-progression costs – JGDG observed	Source: Lilly Observational study	[redacted]	0.89	[redacted]
Source of post-progression costs – JGDG adjusted for follow-up	Source: Lilly Observational study	[redacted]	0.89	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=0.5		[redacted]	0.89	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=1.5	Post-progression costs independent of	[redacted]	0.89	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=2.0	survival post-progression; adjustment factor inactive	[redacted]	0.89	[redacted]
BSA based on JGDG 1.95m^2 Weight based on JGDG 84.2kg	Mean BSA 1.91m^2 Mean weight 77.3 (both based on UK data)	[redacted]	0.89	[redacted]

Proportion of women in cohort as Cancer research UK 49%	JGDG 56%	[redacted]	0.90	[redacted]
Exclude grade 1 and 2 AEs	Includes grade 1 and 2 AEs	[redacted]	0.89	[redacted]
Increase health state costs progression-free by 20%: £157.2	£131	[redacted]	0.89	[redacted]
Decrease health state costs progression-free by 20%: £104.8	£131	[redacted]	0.89	[redacted]
Increase health state costs progressed by 20%: £42	£35	[redacted]	0.89	[redacted]
Decrease health state costs progressed by 20%: £28	£35	[redacted]	0.89	[redacted]
Increase number of administrations for OlaDox : Ola and Dox by 20%: Ola [redacted]; Dox: 6.72	Mean [redacted]	[redacted]	0.89	[redacted]
Decrease number of administrations for Ola and Dox by 20%: Ola: [redacted], Dox 4.48	Mean [redacted]	[redacted]	0.89	[redacted]
Assume Olaratumab SPC dose (15mg/kg)	JGDG mean dose [redacted]/kg	[redacted]	0.89	[redacted]
Utilities				
Increase utility value for progression-free health state by 20%: 0.864	0.72	[redacted]	0.91	[redacted]
Decrease utility value for progression-free health state by 20%: 0.576	0.72	[redacted]	0.87	[redacted]
Increase utility value for progressed health state by 20%: 0.672	0.56	[redacted]	1.05	[redacted]
Decrease utility value for progressed health state by 20%: 0.448	0.56	[redacted]	0.73	[redacted]
Utility value for progression-free state varies with response	Utility values independent of response	[redacted]	0.89	[redacted]
Efficacy				
PFS – Blinded independent review	Investigator assessed	[redacted]	0.88	[redacted]
PFS – parametric survival function Log-normal	KM function	[redacted]	0.90	[redacted]
PFS – parametric survival function Weibull	KM function	[redacted]	0.89	[redacted]
PFS – parametric survival function Gompertz	KM function	[redacted]	0.89	[redacted]
PFS – parametric survival function Gamma	KM function	[redacted]	0.89	[redacted]
Include JGDG KM data up to 47 months	32 months	[redacted]	0.97	[redacted]
Apply In-trial HR indefinitely	Apply HR=1 after trial follow-up	[redacted]	1.56	[redacted]
Taper HR over a defined period (12 months)	Apply HR=1 after trial follow-up	[redacted]	0.98	[redacted]
OS – parametric survival function Log-normal		[redacted]	0.75	[redacted]

OS – parametric survival function Weibull		[redacted]	0.50	[redacted]
OS – parametric survival function Gompertz		[redacted]	0.52	[redacted]
Analysis settings				
Time horizon 20 years	25 years	[redacted]	0.88	[redacted]
Time horizon 15 years	25 years	[redacted]	0.84	[redacted]
Discounting costs at 0%	3.5%	[redacted]	0.89	[redacted]
Discounting health effects at 0%	3.5%	[redacted]	1.06	[redacted]
Discounting costs and effects at 0%	3.5%	[redacted]	1.06	[redacted]
Discounting costs at 6%	3.5%	[redacted]	0.89	[redacted]
Discounting health effects at 6%	3.5%	[redacted]	0.80	[redacted]
Discounting costs and effects at 6%	3.5%	[redacted]	0.80	[redacted]
ITT population*	First-line population	[redacted]	0.66	[redacted]

Source: Eli Lilly submission, table 83, pp. 200-201.

Table A14. Deterministic sensitivity analysis - OlaDox vs IfoDox first-line population at list price

Parameter	Value or assumption in base case	Incr. cost (£)	Incr. benefit (QALY)	ICER (£)
	Base case	[redacted]	0.75	[redacted]
Costs				
Only 500mg vial, no 190mg vial size	Includes 500mg and 190mg vial sizes	[redacted]	0.75	[redacted]
Wastage excluded (assumes vial sharing)	Wastage included	[redacted]	0.75	[redacted]
Exclude dexrazoxane costs	Includes dexrazoxane costs	[redacted]	0.75	[redacted]
OlaDox delivery cost, day 1– Lower quartile £212	Daycase £329	[redacted]	0.75	[redacted]
OlaDox delivery cost , day 1– Upper quartile £400	Daycase £329	[redacted]	0.75	[redacted]
Ola monotherapy day 1– Outpatient lower quartile £119	Daycase £186	[redacted]	0.75	[redacted]
Ola monotherapy day 1– Outpatient upper quartile £203	Daycase £186	[redacted]	0.75	[redacted]
Ola monotherapy day 8– Outpatient lower quartile £107	Outpatient £204	[redacted]	0.75	[redacted]
Ola monotherapy day 8– Outpatient upper quartile £237	Outpatient £204	[redacted]	0.75	[redacted]

Increase IfoDox dose by 20%, 3600 x 3 days	3000mg x 3 days	[redacted]	0.75	[redacted]
Decrease IfoDox dose by 20%, 2400 x 3 days	3000mg x 3 days	[redacted]	0.75	[redacted]
Cardiac monitoring costs - Echo Lower Quartile £119	£153	[redacted]	0.75	[redacted]
Cardiac monitoring costs –Echo Upper quartile £180	£153	[redacted]	0.75	[redacted]
Cardiac monitoring costs – MUGA Upper and Lower quartile £94	£192	[redacted]	0.75	[redacted]
Source of post-progression costs – JGDG observed	Source: Lilly Observational study	[redacted]	0.75	[redacted]
Source of post-progression costs – JGDG adjusted for follow-up	Source: Lilly Observational study	[redacted]	0.75	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=0.5		[redacted]	0.75	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=1.5	Post-progression costs independent of survival post-progression; adjustment factor inactive	[redacted]	0.75	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=2.0		[redacted]	0.75	[redacted]
BSA based on JGDG 1.95m^2 Weight based on JGDG 84.2kg	Mean BSA 1.91m^2 Mean weight 77.3 (both based on UK data)	[redacted]	0.75	[redacted]
Proportion of women in cohort as Cancer research UK 49%	JGDG 56%	[redacted]	0.75	[redacted]
Exclude grade 1 and 2 AEs	Includes grade 1 and 2 AEs	[redacted]	0.76	[redacted]
Increase health state costs progression-free by 20%: £157.2	£131	[redacted]	0.75	[redacted]
Decrease health state costs progression-free by 20%: £104.8	£131	[redacted]	0.75	[redacted]
Increase health state costs progressed by 20%: £42	£35	[redacted]	0.75	[redacted]
Decrease health state costs progressed by 20%: £28	£35	[redacted]	0.75	[redacted]
Increase number of administrations for OlaDox : Ola and Dox by 20%: Ola [redacted]; Dox: 6.72	Mean [redacted]	[redacted]	0.75	[redacted]
Decrease number of administrations for Ola and Dox by 20%: Ola:[redacted], Dox 4.48	Mean [redacted]	[redacted]	0.75	[redacted]
Assume Olaratumab SPC dose (15mg/kg)	JGDG mean dose [redacted]/kg	[redacted]	0.75	[redacted]
Utilities				
Increase utility value for progression-free health state by 20%: 0.864	0.72	[redacted]	0.77	[redacted]

Decrease utility value for progression-free health state by 20%: 0.576		0.72	[redacted]	0.74	[redacted]
Increase utility value for progressed health state by 20%: 0.672		0.56	[redacted]	0.89	[redacted]
Decrease utility value for progressed health state by 20%: 0.448		0.56	[redacted]	0.62	[redacted]
Utility value for progression-free state varies with response	Utility values independent of response		[redacted]	0.74	[redacted]
Efficacy					
Include JGDG KM data up to 47 months	32 months		[redacted]	0.93	[redacted]
Analysis settings					
Time horizon 20 years	25 years		[redacted]	0.73	[redacted]
Time horizon 15 years	25 years		[redacted]	0.68	[redacted]
Discounting costs at 0%	3.5%		[redacted]	0.75	[redacted]
Discounting health effects at 0%	3.5%		[redacted]	0.95	[redacted]
Discounting costs and effects at 0%	3.5%		[redacted]	0.95	[redacted]
Discounting costs at 6%	3.5%		[redacted]	0.75	[redacted]
Discounting health effects at 6%	3.5%		[redacted]	0.65	[redacted]
Discounting costs and effects at 6%	3.5%		[redacted]	0.65	[redacted]
ITT population*	First-line population		[redacted]	0.69	[redacted]

Source: Eli Lilly submission, table 84, pp. 202-203.

Table A15. Deterministic sensitivity analysis - OlaDox vs Dox first-line population at list price

Parameter	Value or assumption in base case	Incr. cost (£)	Incr. benefit (QALY)	ICER (£)
	Base case	[redacted]	**0.89**	[redacted]
Costs				
Only 500mg vial, no 190mg vial size	Includes 500mg and 190mg vial sizes	[redacted]	0.89	[redacted]
Wastage excluded (assumes vial sharing)	Wastage included	[redacted]	0.89	[redacted]
Exclude dexrazoxane costs	Includes dexrazoxane costs	[redacted]	0.89	[redacted]
OlaDox delivery cost, day 1– Lower quartile £212	Daycase £329	[redacted]	0.89	[redacted]
OlaDox delivery cost , day 1– Upper quartile £400	Daycase £329	[redacted]	0.89	[redacted]
Ola monotherapy day 1– Outpatient lower quartile £119	Daycase £186	[redacted]	0.89	[redacted]

Ola monotherapy day 1– Outpatient upper quartile £203	Daycase £186	[redacted]	0.89	[redacted]
Ola monotherapy day 8– Outpatient lower quartile £107	Outpatient £204	[redacted]	0.89	[redacted]
Ola monotherapy day 8– Outpatient upper quartile £237	Outpatient £204	[redacted]	0.89	[redacted]
Cardiac monitoring costs - Echo Lower Quartile £119	£153	[redacted]	0.89	[redacted]
Cardiac monitoring costs –Echo Upper quartile £180	£153	[redacted]	0.89	[redacted]
Cardiac monitoring costs – MUGA Upper and Lower quartile £94	£192	[redacted]	0.89	[redacted]
Source of post-progression costs – JGDG observed	Source: Lilly Observational study	[redacted]	0.89	[redacted]
Source of post-progression costs – JGDG adjusted for follow-up	Source: Lilly Observational study	[redacted]	0.89	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=0.5		[redacted]	0.89	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=1.5	Post-progression costs independent of survival post-progression; adjustment factor inactive	[redacted]	0.89	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=2.0		[redacted]	0.89	[redacted]
BSA based on JGDG 1.95m^2	Mean BSA 1.91m^2	[redacted]	0.89	[redacted]
Weight based on JGDG 84.2kg	Mean weight 77.3 (both based on UK data)			
Proportion of women in cohort as Cancer research UK 49%	JGDG 56%	[redacted]	0.90	[redacted]
Exclude grade 1 and 2 AEs	Includes grade 1 and 2 AEs	[redacted]	0.89	[redacted]
Increase health state costs progression-free by 20%: £157.2	£131	[redacted]	0.89	[redacted]
Decrease health state costs progression-free by 20%: £104.8	£131	[redacted]	0.89	[redacted]
Increase health state costs progressed by 20%: £42	£35	[redacted]	0.89	[redacted]
Decrease health state costs progressed by 20%: £28	£35	[redacted]	0.89	[redacted]
Increase number of administrations for OlaDox : Ola and Dox by 20%: Ola [redacted]; Dox: 6.72	Mean [redacted]	[redacted]	0.89	[redacted]
Decrease number of administrations for Ola and Dox by 20%: Ola:[redacted], Dox 4.48	Mean [redacted]	[redacted]	0.89	[redacted]
Assume Olaratumab SPC dose (15mg/kg)	JGDG mean dose [redacted]/kg	[redacted]	0.89	[redacted]
Utilities				

Increase utility value for progression-free health state by 20%: 0.864	0.72	[redacted]	0.91	[redacted]
Decrease utility value for progression-free health state by 20%: 0.576	0.72	[redacted]	0.87	[redacted]
Increase utility value for progressed health state by 20%: 0.672	0.56	[redacted]	1.05	[redacted]
Decrease utility value for progressed health state by 20%: 0.448	0.56	[redacted]	0.73	[redacted]
Utility value for progression-free state varies with response	Utility values independent of response	[redacted]	0.89	[redacted]
Efficacy				
PFS – Blinded independent review	Investigator assessed	[redacted]	0.88	[redacted]
PFS – parametric survival function Log-normal	KM function	[redacted]	0.90	[redacted]
PFS – parametric survival function Weibull	KM function	[redacted]	0.89	[redacted]
PFS – parametric survival function Gompertz	KM function	[redacted]	0.89	[redacted]
PFS – parametric survival function Gamma	KM function	[redacted]	0.89	[redacted]
Include JGDG KM data up to 47 months	32 months	[redacted]	0.97	[redacted]
Apply In-trial HR indefinitely	Apply HR=1 after trial follow-up	[redacted]	1.56	[redacted]
Taper HR over a defined period (12 months)	Apply HR=1 after trial follow-up	[redacted]	0.98	[redacted]
OS – parametric survival function Log-normal		[redacted]	0.75	[redacted]
OS – parametric survival function Weibull		[redacted]	0.50	[redacted]
OS – parametric survival function Gompertz		[redacted]	0.52	[redacted]
			Analysis settings	
Time horizon 20 years	25 years	[redacted]	0.88	[redacted]
Time horizon 15 years	25 years	[redacted]	0.84	[redacted]
Discounting costs at 0%	3.5%	[redacted]	0.89	[redacted]
Discounting health effects at 0%	3.5%	[redacted]	1.06	[redacted]
Discounting costs and effects at 0%	3.5%	[redacted]	1.06	[redacted]
Discounting costs at 6%	3.5%	[redacted]	0.89	[redacted]
Discounting health effects at 6%	3.5%	[redacted]	0.80	[redacted]
Discounting costs and effects at 6%	3.5%	[redacted]	0.80	[redacted]
*ITT population**	First-line population	[redacted]	0.66	[redacted]

Source: Eli Lilly submission, table 83, pp. 200-201.

Table 1: Deterministic sensitivity analysis - OlaDox vs IfoDox first-line population at list price

Parameter	Value or assumption in base case	Incr. cost (£)	Incr. benefit (QALY)	ICER (£)
	Base case	[redacted]	**0.75**	[redacted]
Costs				
Only 500mg vial, no 190mg vial size	Includes 500mg and 190mg vial sizes	[redacted]	0.75	[redacted]
Wastage excluded (assumes vial sharing)	Wastage included	[redacted]	0.75	[redacted]
Exclude dexrazoxane costs	Includes dexrazoxane costs	[redacted]	0.75	[redacted]
OlaDox delivery cost, day 1– Lower quartile £212	Daycase £329	[redacted]	0.75	[redacted]
OlaDox delivery cost , day 1– Upper quartile £400	Daycase £329	[redacted]	0.75	[redacted]
Ola monotherapy day 1– Outpatient lower quartile £119	Daycase £186	[redacted]	0.75	[redacted]
Ola monotherapy day 1– Outpatient upper quartile £203	Daycase £186	[redacted]	0.75	[redacted]
Ola monotherapy day 8– Outpatient lower quartile £107	Outpatient £204	[redacted]	0.75	[redacted]
Ola monotherapy day 8– Outpatient upper quartile £237	Outpatient £204	[redacted]	0.75	[redacted]
Increase IfoDox dose by 20%, 3600 x 3 days	3000mg x 3 days	[redacted]	0.75	[redacted]
Decrease IfoDox dose by 20%, 2400 x 3 days	3000mg x 3 days	[redacted]	0.75	[redacted]
Cardiac monitoring costs - Echo Lower Quartile £119	£153	[redacted]	0.75	[redacted]
Cardiac monitoring costs –Echo Upper quartile £180	£153	[redacted]	0.75	[redacted]
Cardiac monitoring costs – MUGA Upper and Lower quartile £94	£192	[redacted]	0.75	[redacted]
Source of post-progression costs – JGDG observed	Source: Lilly Observational study	[redacted]	0.75	[redacted]
Source of post-progression costs – JGDG adjusted for follow-up	Source: Lilly Observational study	[redacted]	0.75	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=0.5		[redacted]	0.75	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=1.5	Post-progression costs independent of survival post-progression; adjustment factor inactive	[redacted]	0.75	[redacted]
Post-progression costs vary with post-progression survival, adjustment factor=2.0		[redacted]	0.75	[redacted]

BSA based on JGDG 1.95m²	Mean BSA 1.91m²	[redacted]	0.75	[redacted]
Weight based on JGDG 84.2kg	Mean weight 77.3 (both based on UK data)			
Proportion of women in cohort as Cancer research UK 49%	JGDG 56%	[redacted]	0.75	[redacted]
Exclude grade 1 and 2 AEs	Includes grade 1 and 2 AEs	[redacted]	0.76	[redacted]
Increase health state costs progression-free by 20%: £157.2	£131	[redacted]	0.75	[redacted]
Decrease health state costs progression-free by 20%: £104.8	£131	[redacted]	0.75	[redacted]
Increase health state costs progressed by 20%: £42	£35	[redacted]	0.75	[redacted]
Decrease health state costs progressed by 20%: £28	£35	[redacted]	0.75	[redacted]
Increase number of administrations for OlaDox : Ola and Dox by 20%: Ola [redacted]; Dox: 6.72	Mean [redacted]	[redacted]	0.75	[redacted]
Decrease number of administrations for Ola and Dox by 20%: Ola:[redacted], Dox 4.48	Mean [redacted]	[redacted]	0.75	[redacted]
Assume Olaratumab SPC dose (15mg/kg)	JGDG mean dose [redacted]/kg	[redacted]	0.75	[redacted]
Utilities				
Increase utility value for progression-free health state by 20%: 0.864	0.72	[redacted]	0.77	[redacted]
Decrease utility value for progression-free health state by 20%: 0.576	0.72	[redacted]	0.74	[redacted]
Increase utility value for progressed health state by 20%: 0.672	0.56	[redacted]	0.89	[redacted]
Decrease utility value for progressed health state by 20%: 0.448	0.56	[redacted]	0.62	[redacted]
Utility value for progression-free state varies with response	Utility values independent of response	[redacted]	0.74	[redacted]
Efficacy				
Include JGDG KM data up to 47 months	32 months	[redacted]	0.93	[redacted]
Analysis settings				
Time horizon 20 years	25 years	[redacted]	0.73	[redacted]
Time horizon 15 years	25 years	[redacted]	0.68	[redacted]
Discounting costs at 0%	3.5%	[redacted]	0.75	[redacted]
Discounting health effects at 0%	3.5%	[redacted]	0.95	[redacted]
Discounting costs and effects at 0%	3.5%	[redacted]	0.95	[redacted]
Discounting costs at 6%	3.5%	[redacted]	0.75	[redacted]
Discounting health effects at 6%	3.5%	[redacted]	0.65	[redacted]
Discounting costs and effects at 6%	3.5%	[redacted]	0.65	[redacted]
*ITT population**	First-line population	[redacted]	0.69	[redacted]

Source: Eli Lilly submission, table 84, pp. 202-203.