

CONTRACT AMENDMENT # 1	EMENDAMENTO N. 1 AL CONTRATTO
THIS CONTRACT AMENDMENT # [1] (“ <u>Contract Amendment # 1</u> ”), retrospectively effective as of 24 June 2024 (the “ <u>Effective Date</u> ”), is by and between	IL PRESENTE EMENDAMENTO N. 1 AL CONTRATTO (“ <u>Emendamento n. 1 al contratto</u> ”), con effetto retroattivo al 24 giugno 2024 (la “ <u>Data di decorrenza</u> ”), è stipulato da e tra
ICON CLINICAL RESEARCH LIMITED , a clinical research organisation headquartered in South County Business Park, Leopardstown, Dublin 18, Ireland, European Union, VAT no. IE 8201978R, in the person of legal representative, Dr. Francesco Falcicchio in his capacity as Proxy (hereinafter referred to as the “CRO”) acting as an independent contractor for <i>Pharma Mar S.A.</i> , headquartered in Avda de los Reyes, 1, Polígono Industrial “La Mina”, 28770 Colmenar Viejo (Madrid) Spain, tax code and VAT no. A78267176, as <i>Legal Representative Luis Mora Capitan</i> , in the capacity of Managing Director (hereinafter the “Sponsor”), by virtue of the appropriate power of attorney granted on 30 May 2023.	ICON CLINICAL RESEARCH LIMITED , un'organizzazione di ricerca clinica con sede in South County Business Park, Leopardstown, Dublino 18, Irlanda, Unione Europea, Partita IVA. IE 8201978R, nella persona del legale rappresentante, Dott. Francesco Falcicchio, in qualità di procuratore (d'ora innanzi denominato/a "CRO") agendo come contraente indipendente per <i>Pharma Mar S.A.</i> sito in Avda de los Reyes, 1, Polígono Industrial “La Mina”, 28770 Colmenar Viejo (Madrid) Spagna codice postale e P.IVA A78267176, come <i>Legale Rappresentante Luis Mora Capitan</i> in qualità di Amministratore Delegato (d'ora innanzi denominato/a "Promotore"), in forza di idonea procura conferita in data 30 maggio 2023.
AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO “PAOLO GIACCONE” DI PALERMO (hereinafter referred to as the “Entity”), with registered office in PALERMO Via del Vespro 129 C.F. and P. IVA n. 05841790826, in the person of the Director General, Dr. Maria Grazia Furnari, with appropriate powers to sign this act	AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO “PAOLO GIACCONE” DI PALERMO (d'ora innanzi denominato/a “Ente”), con sede legale in PALERMO Via del Vespro 129 C.F. e P. IVA n. 05841790826, in persona della Direttrice Generale, Dott.ssa Maria Grazia Furnari, munita di idonei poteri di firma del presente atto
WITNESSETH:	ATTESTA:
WHEREAS , under the terms of a certain Clinical Trial Agreement, dated 7 December 2023, and as amended (the “ <u>Agreement</u> ”) between and among the parties, Sponsor retained the Entity and Investigator to perform the research study entitled ““Randomized, Controlled, Open-label, Phase IIb/III Study of Lurbinectedin in Combination with Doxorubicin versus Doxorubicin Alone as First-line Treatment in Patients with	PREMESSO CHE , in base ai termini di una specifica Convenzione di sperimentazione clinica, datata 7 dicembre 2023 e successivi emendamenti (la “ <u>Convenzione</u> ”) in essere tra le parti, il Promotore ha incaricato l'Ente e lo Sperimentatore di condurre lo studio di ricerca intitolato “Studio randomizzato, controllato, in aperto, di fase IIb/III su lurbinectedina in combinazione con doxorubicina rispetto a

Metastatic Leiomyosarcoma" (the " <u>Study</u> "), sponsored by the Sponsor Pharma Mar, S.A., as more particularly described in the Agreement; and	doxorubicina in monoterapia come trattamento di prima linea in pazienti con leiomiomasarcoma metastatico" (lo " <u>Studio</u> "), sponsorizzato dallo sponsor Pharma Mar, S.A., come descritto più dettagliatamente nella Convenzione; e
WHEREAS , the parties hereto have entered into certain additional agreements with respect to modification of the Agreement, and which they desire to memorialize in this Contract Amendment # [1];	PREMESSO CHE le parti contraenti hanno stipulato alcuni accordi aggiuntivi relativamente alla modifica della Convenzione, che desiderano formalizzare nel presente Emendamento n. [1] al contratto;
WHEREAS ICON Clinical research Limited with place of business at South County Business Park, Leopardstown, Dublin 18, Ireland and its affiliates (" ICON ") have been duly authorized by the Sponsor to conduct certain obligations of the Sponsor with regard to the clinical trial detailed below, in accordance with the terms and conditions herein as well as to sign this Amendment in the name and on behalf of the Sponsor.	PREMESSO CHE ICON Clinical Research Limited la cui sede di attività è ubicata a South County Business Park, Leopardstown, Dublin 18, Irlanda e le sue consociate (" ICON ") sono state debitamente autorizzate dal Promotore ad adempiere determinati obblighi del Promotore relativi alla sperimentazione clinica specificata di seguito, in conformità ai termini e alle condizioni ivi previsti nonché a firmare il presente Emendamento in nome e per conto del Promotore.
WHEREAS, Protocol version 4.0 dated 21 March 2024 was authorized on 24 June 2024 in Italy under Regulation (EU) No 536/2014;	PREMESSO CHE il Protocollo versione 4.0 del 21 marzo 2024 è stato autorizzato in Italia il 24 giugno 2024 ai sensi del Regolamento (UE) n. 536/2014;
NOW, THEREFORE , in consideration of the premises and of the following mutual promises, covenants and conditions hereinafter set forth, the parties hereto agree as follows:	TUTTO CIÒ PREMESSO e tenuto conto delle premesse e delle pattuizioni, degli impegni e delle condizioni reciproci ivi contenuti, le parti convengono quanto segue:
1. Budget /Payment Schedule. To account for changes to the services and costs updated on Protocol version 4.0 dated 21 March 2024 under the Agreement, the parties agree that the Budget attached to the Agreement as Annex A is hereby deleted in its entirety and replaced by the Revised Budget attached hereto as Appendix A .	1. Budget / Schema di pagamento. Al fine di tener conto delle modifiche ai servizi e ai costi aggiornati alla versione 4.0 del Protocollo del 21 marzo 2024 nell'ambito della Convenzione, le parti convengono che il Budget allegato alla Convenzione come Allegato A viene eliminato nella sua interezza e sostituito dal Budget rivisto allegato al presente documento come Allegato A .
2. Ratification of Balance of Agreement. In all other respects, the terms of	2. Ratifica della restante parte della Convenzione. Per tutti gli altri aspetti, i termini della Convenzione sono con il presente

the Agreement are hereby ratified and affirmed by each of the parties hereto.	ratificati e confermati da ciascuna delle parti del presente.
3. Headings. The headings in this Contract Amendment # 1 are for convenience of reference only and shall not affect its interpretation.	3. Intestazioni. Le intestazioni del presente Emendamento n. 1 al contratto sono esclusivamente per comodità di riferimento e non devono comprometterne l'interpretazione.
IN WITNESS WHEREOF, the parties hereto, each by a duly authorized representative, have executed this Contract Amendment # 1 as of the date indicated below, but effective for all purposes as of the Effective Date.	A TESTIMONIANZA DI CIÒ, le parti, ciascuna per il tramite di un rappresentante debitamente autorizzato, hanno reso esecutivo il presente Emendamento n. 1 al contratto alla data indicata di seguito, ma efficace a tutti gli effetti a partire dalla Data di Efficacia.

For the Entity / Per l'Ente

Dott.ssa Maria Grazia Furnari
General Director/Direttrice Generale

Firma/Signature, Data/Date _____

For ICON CLINICAL RESEARCH LIMITED / Per ICON CLINICAL RESEARCH LIMITED

Francesco Falcicchio
The Proxy/Il procuratore

Firma/Signature, Data/Date _____

APPENDIX A REVISED BUDGET	ALLEGATO A BUDGET RIVISTO
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Trial Information

Trial Name: PharmaMar_PAM18310-183010
Project: PAM18310-183010
Protocol Number: PM1183-C-010-22
Protocol Version: Protocol 4.0 dated 21 March 2024
Phase: Ib/III
Title: Randomized, Controlled, Open-label, Phase Ib/III Study of Lurbinectedin in Combination with Doxorubicin versus Doxorubicin Alone as First-line Treatment in Patients with Metastatic Leiomyosarcoma
Arm: Control Arm

Budget Information

Location: Italy
Currency: EUR - Euro
Total Cost per Patient Control Arm: 6,768.00
PI Name: Dr Badalamenti
Site Name: Policlinico P. Giaccone - Palermo
Overhead Percent: 0.00%

Procedure Name	Selected Cost	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6 (and beyond) +D1	EOT*	Follow-up
Signed and dated written informed consent	58.00	58.00													
Informed Consent : PGx substudy (optional)	55.00	Invoice													
Confirmation of eligibility and inclusion	37.00	37.00	37.00												
Initial visit w Physical Exam, Demographic, Medical / Cancer, Height, Weight , BSA and Vital Signs	191.00	191.00													
Follow-up visit w Complete Physical Exam, Weight, BSA (if required) and Vital Signs	96.00		Invoice				96.00			96.00	96.00	96.00	96.00	96.00	
ECOG PS	11.00	11.00	Invoice				11.00			11.00	11.00	11.00	11.00	11.00	
Local Lab : Hematology	15.00	15.00	Invoice		15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00
Local Lab: Hemoglobin	18.00	18.00	Invoice		18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00
Local Lab : Biochemistry A	67.00	67.00	Invoice		67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00
Local Lab : Biochemistry A - CPK	9.00	9.00	Invoice		9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00
Local Lab : Biochemistry B	33.00	33.00	Invoice				33.00			33.00	33.00	33.00	33.00	33.00	33.00
Local Lab : Biochemistry B- Cardiac Serum Biomarkers	25.00	25.00	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
Local Lab : Biochemistry B- CRP	15.00	15.00	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
ECG	61.00	61.00								Invoice					
LVEF assessment MUGA	250.00	Invoice													
LVEF assessment ECHO	230.00	Invoice													
Local Lab : Pregnancy test (if applicable)	Invoice	Invoice	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
Doxorubicin infusion	77.00		77.00				77.00			77.00	77.00	77.00	77.00	77.00	
Central Lab : Blood draw: Pharmacokinetics, AAG and IL-6 (only in Cycle 1)	63.00		315.00	63.00			Invoice								
Blood Sample Handling, Preparation and Shipment to Central Lab	54.00		54.00	54.00			Invoice								
Archived FFPE tumor tissue	30.00									Invoice					
Clinical and radiological tumor assessment	Invoice	Invoice								Invoice					Invoice
EORTC QLQ-C30	26.00	26.00								Invoice					
Concomitant therapies	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00
Adverse events	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00
Survival follow up / Telephone call	20.00														20.00
Per Patient Activity Totals:		602.00	519.00	153.00	145.00	145.00	362.00	145.00	145.00	362.00	362.00	362.00	362.00	285.00	56.00

* All assessments at EoT will only repeat procedures which occurred > 10 days before

Non-Procedure Name	Selected Cost	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6 (and beyond) +D1	EOT*	Follow-up
Pharmacy Dispense - Doxorubicin	51.00		51.00				51.00			51.00	51.00	51.00	51.00		
Physician's Fee	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	39.50
Study Coordinator fee	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	35.00
Data Entry	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	16.50
Per Patient Other Direct Cost Totals:		182.00	233.00	182.00	182.00	182.00	233.00	182.00	182.00	233.00	233.00	233.00	233.00	182.00	91.00

	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6 (and beyond) +D1	EOT*	Follow-up
Visit Cost Subtotal	784.00	752.00	335.00	327.00	327.00	595.00	327.00	327.00	595.00	595.00	595.00	595.00	467.00	147.00
Overhead at 0%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total Cost Per Visit	784.00	752.00	335.00	327.00	327.00	595.00	327.00	327.00	595.00	595.00	595.00	595.00	467.00	147.00
Visit Quantity	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Cumulative Visit Cost	784.00	752.00	335.00	327.00	327.00	595.00	327.00	327.00	595.00	595.00	595.00	595.00	467.00	147.00
Total Cost per Patient Control Arm:	6,768.00													

Trial Information

Trial Name: PharmaMar_PAM18310-183010
Project: PAM18310-183010
Protocol Number: PM1183-C-010-22
Protocol Version: Protocol 4.0 dated 21 March 2024
Phase: IIb/III
Title: Randomized, Controlled, Open-label, Phase IIb/III Study of Lurbinectedin in Combination with Doxorubicin versus DoxorubicinAlone as First-line Treatment in Patients with Metastatic Leiomyosarcoma

Arm: Experimental
 Arm A

Budget Information

Location: Italy
Currency: EUR - Euro
Total Cost Per Patient Experimental Arm A: 11,981.00

PI Name: Dr Badalamenti
Site Name: Policlinico P. Giaccone - Palermo
Overhead Percent: 0.00%

Procedure Name	Selected Cost	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13(and beyond) +D1	EOT	Follow-up	
Signed and dated written informed consent	58.00	58.00																					
Informed Consent : PqX substudy (optional)	55.00	Invoice																					
Confirmation of eligibility and inclusion	37.00	37.00	37.00																				
Initial visit w Physical Exam, Demographic, Medical /	191.00	191.00																					
Follow-up visit w Complete Physical Exam, Weight, ECOG PS	96.00	96.00	Invoice				96.00			96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00
Local Lab : Hematology	15.00	15.00	Invoice		15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00
Local Lab: Hemoglobin	18.00	18.00	Invoice		18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00
Local Lab : Biochemistry A	67.00	67.00	Invoice		67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00
Local Lab : Biochemistry A - CPK	9.00	9.00	Invoice		9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00
Local Lab : Biochemistry B	33.00	33.00	Invoice				33.00			33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00
Local Lab : Biochemistry B- Cardiac Serum	25.00	25.00	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
Local Lab : Biochemistry B- CRP	15.00	15.00	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
ECG	61.00	61.00																					
LVEF assessment MUGA	250.00	Invoice																					
LVEF assessment ECHO	230.00	Invoice																					
Local Lab : Pregnancy test (if applicable)	Invoice	Invoice	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
Doxorubicin infusion	77.00	77.00	77.00				77.00			77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00
Lurbinectedin Infusion	70.00	70.00	70.00				70.00			70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00
Central Lab : Blood draw: Pharmacokinetics, AAG and IL-6 (only in Cycle 1)	63.00	63.00	315.00	63.00			Invoice																
Blood Sample Handling, Preparation and Shipment to Central Lab	54.00	54.00	54.00	54.00			Invoice																
Archived FFPE tumor tissue	30.00																						
Clinical and radiological tumor assessment	Invoice	Invoice																					
EORTC QLQ-C30	26.00	26.00																					
Concomitant therapies	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00
Adverse events	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00
Survival follow up / Telephone call	20.00	20.00																					20.00
Per Patient Activity Totals:		602.00	589.00	153.00	145.00	145.00	432.00	145.00	145.00	432.00	432.00	432.00	432.00	432.00	432.00	432.00	355.00	355.00	355.00	355.00	285.00	56.00	

Non-Procedure Name	Selected Cost	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13(and beyond) +D1	EOT	Follow-up	
Pharmacy Dispense - Doxorubicin	51.00		51.00				51.00			51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00
Pharmacy Dispense - Lurbinectedin	50.00		50.00				50.00			50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00
Physician's Fee	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	39.50
Study Coordinator fee	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	35.00
Data Entry	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	16.50
Per Patient Other Direct Cost Totals:		182.00	283.00	182.00	182.00	182.00	283.00	182.00	182.00	283.00	283.00	283.00	283.00	283.00	283.00	283.00	232.00	232.00	232.00	232.00	182.00	91.00	

	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13(and beyond) +D1	EOT	Follow-up	
Visit Cost Subtotal	784.00	872.00	335.00	327.00	327.00	715.00	327.00	327.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	587.00	587.00	587.00	587.00	467.00	147.00	
Overhead at 0%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total Cost Per Visit	784.00	872.00	335.00	327.00	327.00	715.00	327.00	327.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	587.00	587.00	587.00	587.00	467.00	147.00	
Visit Quantity	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Cumulative Visit Cost	784.00	872.00	335.00	327.00	327.00	715.00	327.00	327.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	587.00	587.00	587.00	587.00	467.00	147.00	
Total Cost Per Patient Experimental Arm A:		11,981.00																				

Trial Information

Trial Name: PharmaMar_PAM18310-183010
Project: PAM18310-183010
Protocol Number: PM1183-C-010-22
Protocol Version: Protocol 4.0 dated 21 March 2024
Phase: IIb/III
Title: Randomized, Controlled, Open-label, Phase IIb/III Study of Lurbinectedin in Combination with Doxorubicin versus Doxorubicin
 Alone as First-line Treatment in Patients with Metastatic Leiomyosarcoma
Arm: Experimental Arm B

Budget Information

Location: Italy
Currency: EUR - Euro
Total Cost per Patient Experimental Arm B: 12,241.00
PI Name: Dr Badalamenti
Site Name: Policlinico P.
Overhead Percent: 0.00%

Procedure Name	Selected Cost	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13(and Beyond) +D1	EOT	Follow-up
Signed and dated written informed consent	58.00	58.00																				
Informed Consent : PGx substudy (optional)	55.00	Invoice																				
Confirmation of eligibility and inclusion	37.00	37.00	37.00																			
Initial visit w Physical Exam, Demographic,	191.00	191.00																				
Follow-up visit w Complete Physical Exam,	96.00		Invoice				96.00			96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00	96.00
ECOG PS	11.00	11.00	Invoice				11.00			11.00	11.00	11.00	11.00	11.00	11.00	11.00	11.00	11.00	11.00	11.00	11.00	11.00
Local Lab : Hematology	15.00	15.00	Invoice		15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00
Local Lab : Hemoglobin	18.00	18.00	Invoice		18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00	18.00
Local Lab : Biochemistry A	67.00	67.00	Invoice		67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00	67.00
Local Lab : Biochemistry A - CPK	9.00	9.00	Invoice		9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00	9.00
Local Lab : Biochemistry B	33.00	33.00	Invoice				33.00			33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00
Local Lab : Biochemistry B- Cardiac Serum	25.00	25.00	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
Local Lab : Biochemistry B- CRP	15.00	15.00	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
ECG	61.00	61.00																				
LVEF assessment MUGA	250.00	Invoice																				
LVEF assessment ECHO	230.00	Invoice																				
Local Lab : Pregnancy test (if applicable)	Invoice	Invoice	Invoice				Invoice			Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice	Invoice
Doxorubicin infusion	77.00		77.00				77.00			77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	77.00	
Lurbinectedin Infusion	70.00		70.00				70.00			70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	
Central Lab : Blood draw: Pharmacokinetics,	63.00		63.00	63.00			Invoice															
Blood Sample Handling, Preparation and	54.00		54.00	54.00			Invoice															
Archived FFPE tumor tissue	30.00																					
Clinical and radiological tumor assessment	Invoice	Invoice																				Invoice
EORTC QLQ-C30	26.00	26.00																				
Concomitant therapies	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00	19.00
Adverse events	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00
Survival follow up / Telephone call	20.00																					20.00
Per Patient Activity Totals:		602.00	337.00	153.00	145.00	145.00	432.00	145.00	145.00	432.00	432.00	432.00	432.00	432.00	432.00	432.00	432.00	432.00	432.00	432.00	285.00	56.00

Non-Procedure Name	Selected Cost	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13(and Beyond) +D1	EOT	Follow-up	
Pharmacy Dispense - Doxorubicin	51.00		51.00				51.00			51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00	51.00			
Pharmacy Dispense - Lurbinectedin	50.00		50.00				50.00			50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00			
Physician's Fee	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	79.00	39.50
Study Coordinator fee	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	70.00	35.00
Data Entry	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	33.00	16.50
Per Patient Other Direct Cost Totals:		182.00	283.00	182.00	182.00	182.00	283.00	182.00	182.00	283.00	283.00	283.00	283.00	283.00	283.00	283.00	283.00	283.00	283.00	283.00	283.00	182.00	91.00

	Screening	C1D1	C1D5	C1D8	C1D15	C2D1	C2D8	C2D15	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13(and Beyond) +D1	EOT	Follow-up
Visit Cost Subtotal	784.00	620.00	335.00	327.00	327.00	715.00	327.00	327.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	467.00	147.00
Overhead at 0%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total Cost Per Visit	784.00	620.00	335.00	327.00	327.00	715.00	327.00	327.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	467.00	147.00
Visit Quantity	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Cumulative Visit Cost	784.00	620.00	335.00	327.00	327.00	715.00	327.00	327.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	715.00	467.00	147.00
Total Cost per Patient Experimental Arm B:	12,241.00																				

Budget Information

Location: Italy
 Currency: EUR - Euro
 Total Cost per Patient Control Arms: 6,768.00
 Total Cost Per Patient Experimental Arm A: 11,981.00
 Total Cost per Patient Experimental Arm B: 12,241.00

PI Name: Dr Badalamenti
 Site Name: Policlinico P. Giaccone - Palermo
 Overhead Percent: 0.00%

Control Arm					
Visit Name	Visit Cost Subtotal	Overhead at 0%	Total Cost Per Visit	Visit Quantity	Cumulative Visit Cost
Screening	784.00	0.00	784.00	1.00	784.00
C1D1	752.00	0.00	752.00	1.00	752.00
C1D5	335.00	0.00	335.00	1.00	335.00
C1D8	327.00	0.00	327.00	1.00	327.00
C1D15	327.00	0.00	327.00	1.00	327.00
C2D1	595.00	0.00	595.00	1.00	595.00
C2D8	327.00	0.00	327.00	1.00	327.00
C2D15	327.00	0.00	327.00	1.00	327.00
C3D1	595.00	0.00	595.00	1.00	595.00
C4D1	595.00	0.00	595.00	1.00	595.00
C5D1	595.00	0.00	595.00	1.00	595.00
C6 (and beyond) +D1	595.00	0.00	595.00	1.00	595.00
EOT*	467.00	0.00	467.00	1.00	467.00
Follow-up	147.00	0.00	147.00	1.00	147.00
Total Cost per Patient Control Arm:					6,768.00

Experimental Arm A					
Visit Name	Visit Cost Subtotal	Overhead at 0%	Total Cost Per Visit	Visit Quantity	Cumulative Visit Cost
Screening	784.00	0.00	784.00	1.00	784.00
C1D1	872.00	0.00	872.00	1.00	872.00
C1D5	335.00	0.00	335.00	1.00	335.00
C1D8	327.00	0.00	327.00	1.00	327.00
C1D15	327.00	0.00	327.00	1.00	327.00
C2D1	715.00	0.00	715.00	1.00	715.00
C2D8	327.00	0.00	327.00	1.00	327.00
C2D15	327.00	0.00	327.00	1.00	327.00
C3D1	715.00	0.00	715.00	1.00	715.00
C4D1	715.00	0.00	715.00	1.00	715.00
C5D1	715.00	0.00	715.00	1.00	715.00
C6D1	715.00	0.00	715.00	1.00	715.00
C7D1	715.00	0.00	715.00	1.00	715.00
C8D1	715.00	0.00	715.00	1.00	715.00
C9D1	715.00	0.00	715.00	1.00	715.00
C10D1	587.00	0.00	587.00	1.00	587.00
C11D1	587.00	0.00	587.00	1.00	587.00
C12D1	587.00	0.00	587.00	1.00	587.00
C13(and beyond) +D1	587.00	0.00	587.00	1.00	587.00
EOT	467.00	0.00	467.00	1.00	467.00
Follow-up	147.00	0.00	147.00	1.00	147.00
Total Cost Per Patient Experimental Arm A:					11,981.00

Experimental Arm B					
Visit Name	Visit Cost Subtotal	Overhead at 0%	Total Cost Per Visit	Visit Quantity	Cumulative Visit Cost
Screening	784.00	0.00	784.00	1.00	784.00
C1D1	620.00	0.00	620.00	1.00	620.00
C1D5	335.00	0.00	335.00	1.00	335.00
C1D8	327.00	0.00	327.00	1.00	327.00
C1D15	327.00	0.00	327.00	1.00	327.00
C2D1	715.00	0.00	715.00	1.00	715.00
C2D8	327.00	0.00	327.00	1.00	327.00
C2D15	327.00	0.00	327.00	1.00	327.00
C3D1	715.00	0.00	715.00	1.00	715.00
C4D1	715.00	0.00	715.00	1.00	715.00
C5D1	715.00	0.00	715.00	1.00	715.00
C6D1	715.00	0.00	715.00	1.00	715.00
C7D1	715.00	0.00	715.00	1.00	715.00
C8D1	715.00	0.00	715.00	1.00	715.00
C9D1	715.00	0.00	715.00	1.00	715.00
C10D1	715.00	0.00	715.00	1.00	715.00
C11D1	715.00	0.00	715.00	1.00	715.00
C12D1	715.00	0.00	715.00	1.00	715.00
C13(and Beyond) +D1	715.00	0.00	715.00	1.00	715.00
EOT	467.00	0.00	467.00	1.00	467.00
Follow-up	147.00	0.00	147.00	1.00	147.00
Total Cost per Patient Experimental Arm B:					12,241.00

Invoiceable Name	Selected Cost	Overhead at 0%	Total Cost	Considerations
Informed Consent : PGx substudy (optional)	55.00	0.00	55.00	For separate Optional PGx Substudy ICF
Follow-up visit w Complete Physical Exam, Weight, BSA (if required) and Vital Signs	96.00	0.00	96.00	
ECOG PS	11.00	0.00	11.00	Repeat if assessed >7 days before Day 1 of Cycle 1 and whenever clinically required as per protocol
Local Lab : Hematology	15.00	0.00	15.00	
Local Lab: Hemoglobin	18.00	0.00	18.00	
Local Lab : Biochemistry A	67.00	0.00	67.00	
Local Lab : Biochemistry A - CPK	9.00	0.00	9.00	
Local Lab : Biochemistry B	33.00	0.00	33.00	
ECG	61.00	0.00	61.00	Repeat if clinically indicated
LVEF assessment MUGA	250.00	0.00	250.00	
LVEF assessment ECHO	230.00	0.00	230.00	Once a minimum cumulative doxorubicin dose is reached as per Protocol, repeat before the next study treatment infusion. Also repeat once the maximum cumulative doxorubicin dose is reached, or at EOT visit (whichever occurs first). Additional LVEF assessments could be performed at the Investigator's discretion
Serum Pregnancy test	21.00	0.00	21.00	Only WOCBP
Urine pregnancy Test	17.00	0.00	17.00	
Pregnancy confirmation Ultrasound	140.00	0.00	140.00	In order to rule out pregnancy as per Protocol
Central Lab : Blood draw: Pharmacokinetics, AAG and IL-6 (only in Cycle 1)	63.00	0.00	63.00	if repeat Blood Draws are required; 2) To assess molecular response as per Protocol; 3) at time of radiological disease progression
Central Lab : Blood draw:Pharmacogenomics-PGx	63.00	0.00	63.00	For patients who have signed separate consent for the PGx substudy
Blood Sample Handling, Preparation and Shipment to Central Lab	54.00	0.00	54.00	Whenever Central Lab Blood draw is collected.
Archived FFPE tumor tissue	30.00	0.00	30.00	Available archived FFPE as per protocol including from patients undergoing resection while on study
Chest CT Scan w/ Contrast	492.00	0.00	492.00	Every six weeks (± 7 days) during the first four months after randomization, every nine weeks (± 14 days) during the next eight months, and every 12 weeks (± 14 days) subsequently as per Protocol
Abdomen CT Scan w/ Contrast	520.00	0.00	520.00	
Pelvic CT Scan w/ Contrast	436.00	0.00	436.00	
Neck CT Scan w/ Contrast	800.00	0.00	800.00	
MRI of Chest w/ Contrast	800.00	0.00	800.00	
MRI of Abdomen w Contrast	800.00	0.00	800.00	
Pelvic MRI w/ Contrast	800.00	0.00	800.00	
Brain MRI With Contrast	525.00	0.00	525.00	
RECIST v.1.1	158.00	0.00	158.00	
Central Imaging Sending	30.00	0.00	30.00	
EORTC QLQ-C30	26.00	0.00	26.00	Every six weeks (± 7 days) during the first four months after randomization, every nine weeks (± 14 days) during the next eight months, and every 12 weeks (± 14 days) subsequently as per Protocol
Prophylactic medication: Subcutaneous G-CSFs, Dexamethasone and Ondansetron			Invoice (market price)	On D1 of each cycle as per protocol and Only for the Experimental Arm and for Control Arm as per Investigator's judgement
Patient Travel Reimbursement			Invoice	Patient will be reimbursed to cover reasonable travel expenses up to 75 EUR per visit incurred as a result of participating in the study. Patient travel reimbursement will be based on actuals upon the provision of a detailed invoice and receipts up to the rates set forth in the Appendix A. In the case that expected actual travel costs of a patient will exceed the herein approved amount per patient and visit, the site agrees to request approval from Sponsor for the reimbursement of such costs in advance prior patient's inclusion.
Local Lab : Biochemistry B- Cardiac Serum Biomarkers	25.00	0.00	25.00	Mandatory at Screening and then repeated if clinically indicated as per Protocol
Local Lab : Biochemistry B- CRP	15.00	0.00	15.00	Mandatory at Screening and then repeated if clinically indicated as per Protocol
Pharmacy Investigation Experimentation	500 €	0.00	500.00	Once
Pharmacy SIV	150.00	0.00	150.00	Once
Pharmacy Fee for each supply	50 €	0.00	50.00	Per shipment (includes quality and quantity control of each
Pharmacy Monitoring visit	100.00	0.00	100.00	For each monitoring visit
Pharmacy Closing visit	150.00	0.00	150.00	Once
Drugs site destroy	55.00	0.00	55.00	Once
Assignment , set up and delivery of infusion drugs	100.00	0.00	100.00	Activities of assigning Kits and dispensing infusion drugs

Site Administrative Fee Name	Total Cost
Site Start-up Costs	1,000.00
EC Payment	2,000.00
Archiving/Document storage (for all the time that the current legislation establishes requires)	950.00

Screening Failure(s)	SF will be billed to Sponsor at 765 EUR for a maximum of 3 patients.
Unscheduled Visit(s)	Unscheduled Visits will be reimbursed per procedure at the rates listed in the Appendix A plus OH on receipt of a detailed invoice.