Trodelvy®

(Sacituzumab govitecan)

Authorization Number: 68179
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Clinical Study Results

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1. INTRODUCTION

As of 2020, Gilead discloses clinical study results of newly authorized products in Switzerland by Swissmedic according to the requirements laid out in Art. 71-73 TPO (Ordinance on Therapeutic Products).

Below you will find the information for clinical studies relevant for the marketing authorization for Trodelvy® (Sacituzumab govitecan) in Switzerland.

2. OVERVIEW ON CLINICAL STUDIES

Study number	Study title:	Indication:	EudraCT-Number:
IMMU-132-05	An International, Multi-Center, Open-Label, Randomized, Phase III Trial of Sacituzumab Govitecan versus Treatment of Physician Choice in Patients with Metastatic Triple-Negative Breast Cancer Who Received at Least Two Prior Treatments.	mTNBC	2017-003019-21

3. STUDY SYNOPSIS IMMU-132-05

Name of Sponsor/Company: Immunomedics, Inc **Name of Finished Product:** **Name of Active Ingredient:** Sacituzumab govitecan (SG)	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Title of Study: An international, multi-center, open-label, randomized, Phase 3 trial of SG versus treatment of physician choice (TPC) in subjects with metastatic triple-negative breast cancer (TNBC) who received at least two prior treatments		
Investigators: 85 investigators		
Study centers: 85 study centers in Belgium, Canada, France, Germany, Spain, the United Kingdom, and the United States		
Publications (reference):		
Studied period (years): Date first subject enrolled: 07 November 2017 Date last subject completed: based on data cut-off date of 11 March 2020		**Phase of development:** Phase 3

Objectives:

Primary Objective:

The primary objective of the study was to compare the efficacy of SG to TPC as measured by an independently-reviewed progression free survival (PFS) in subjects with locally-advanced or metastatic TNBC previously treated with at least 2 systemic chemotherapy regimens for unresectable, locally-advanced or metastatic disease and without brain metastasis at baseline.

Secondary Objectives:

The secondary objectives of the study were to compare the 2 groups for the following:

- PFS for the Intent-to-Treat (ITT) Population
- Overall survival (OS) in both the ITT Population and in the subgroup with brain metastasis
- Independently-determined objective response rate (ORR), duration of response (DOR), and time to onset of response according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1
- Quality of life (QOL)
- Safety, including adverse events (AEs), safety laboratories and evaluations, incidence of dose delays and dose reductions, and treatment discontinuations due to AEs

Methodology:

This study was a Phase 3, randomized, open-label, multicenter study of the efficacy and safety of SG in subjects with either locally-advanced or metastatic TNBC who were either refractory or had relapsed after at least 2 prior standard-of-care chemotherapy regimens. All subjects must also have received previous taxane treatment in either the adjuvant, neoadjuvant, or advanced stage. Subjects who either had a contraindication or were intolerant to taxanes were enrolled if they had received at least 1 cycle of a taxane, with either the contraindication or intolerance during or at the end of the first taxane cycle. Poly-ADP ribose polymerase (PARP) inhibitors were allowed as 1 of 2 prior standard of care chemotherapies for subjects with a documented germ-line BRCA1/BRCA2 mutation. Subjects were enrolled and randomized 1:1 to either SG or TPC (eribulin, capecitabine, gemcitabine, or vinorelbine), with randomization stratified by the number of prior treatments for advanced disease (2-3 versus >3); geographic location (North America versus rest of world); and known brain metastasis at baseline (yes or no). The number of subjects with brain metastasis was limited at 15%.

Tumor response was assessed by computed tomography (CT) or magnetic resonance imaging (MRI) every 6 weeks (same imaging method throughout the study) for 9 months and then every 9 weeks thereafter until the occurrence of progression of disease requiring discontinuation of further treatment. All available CT or MRI

scans were reviewed by the Independent Review Committee (IRC). The decision to discontinue a subject for progressive disease (PD) was made by the investigator. Subjects who discontinued treatment because of toxicity continued with tumor response assessments until progression of disease or initiation of new therapy.

During study conduct, data were monitored by an independent Data Monitoring Committee (DMC). The DSMB met 4 times during the course of the study: 25 May 2018, 02 November 2018, 29 April 2019, and 27 March 2020. Following the meeting of 27 March 2020, the DMC recommended that the study be stopped and the final analysis of data conducted. At this time, 302 of the 315 prespecified events of PFS and 316 of the 330 prespecified events of OS had occurred (ie, 96% of each event). The Sponsor accepted the DMC's recommendation and informed the US Food and Drug Administration (FDA) of the DMC's recommendation; FDA was also provided with the data package reviewed by the DMC. FDA requested that the Statistical Analysis Plan be amended to specify the number of PFS events that would be used for the final analysis and to adjust the 2-sided alpha level for the primary analysis of PFS.

Number of subjects (planned and analyzed):
Planned: 488 subjects
Analyzed: 529 subjects

Diagnosis and main criteria for inclusion:
Male and female subjects, ≥18 years of age, with either locally-advanced or metastatic TNBC who were either refractory or had relapsed after at least 2 prior standard-of-care chemotherapy regimens.

Test product, dose and mode of administration, batch number:

SG 10 mg/kg was administered as an intravenous (IV) infusion; Batch numbers: S17C001, S17H003, S17N001, S18F023, and S18M010.

Comparator, dose and mode of administration:
Eribulin was administered IV over 2 to 5 minutes at a dose 1.4 mg/m^2 at North American sites and 1.23 mg/m^2 at European sites on Days 1 and 8 of a 21-day cycle.
Capecitabine 1,000 to 1,250 mg/m^2 was administered in a 21-day cycle, with capecitabine administered orally twice daily for 2 weeks followed by 1-week rest period.
Gemcitabine 800-1,200 mg/m^2 was administered IV over 30 minutes on Days 1, 8, and 15 of a 28-day cycle.
Vinorelbine 25 mg/m^2 was administered as a weekly IV injection over 6-10 minutes.

Duration of treatment:
Treatment was continued until disease progression or unacceptable toxicity.

Criteria for evaluation:

Efficacy

Primary Efficacy Endpoint:
PFS by Independent Review Committee (IRC) assessment in subjects without brain metastasis at baseline (ie, brain metastasis negative [BM-ve]), defined as the time from randomization until objective tumor progression by RECIST v1.1 or death, whichever came first.

Secondary Efficacy Endpoints:

- PFS by IRC assessment for ITT Population
- OS, defined as the time from the start of study treatment to death from any cause in both the BM-ve Population and ITT Population
- ORR by IRC and investigator assessment, defined as the percentage of subjects who had a confirmed complete response (CR) or partial response (PR)
- Time to response by the IRC and the investigator, defined as the time from randomization to the first recorded objective response (ie, CR or PR)
- DOR by IRC and investigator assessment, defined as the number of days between the first date showing a documented response of CR or PR and the date of progression or death
- Clinical benefit rate (CBR) by IRC and investigator assessment, defined as the percentage of subjects with either CR, PR, or stable disease (SD) with a duration of ≥6 months

Safety Endpoints:
Safety endpoints included AEs, serious AEs (SAEs), AEs leading to permanent discontinuation of study drug, a dose reduction, or a dose interruption, clinical laboratory parameters, vital signs, and electrocardiograms (ECGs).

Statistical methods:
Analysis Populations:
Data were summarized for the following analysis populations:

- BM-ve ITT Population: All subjects without brain metastasis who were randomized to the strata of no baseline brain metastasis; this is the primary analysis population for efficacy
- ITT Population: All subjects who were randomized, with subjects analyzed based on randomized treatment assignment. This population was used for efficacy analyses after the primary endpoint was tested in the primary analysis population of subjects without brain metastases
- Safety Population: All subjects who received at least 1 dose of SG or TPC

Efficacy Endpoints:
The overall Type I error rate was strictly controlled by a hierarchical testing strategy. The primary endpoint of PFS by IRC assessment was analyzed and tested first in BM-ve Population. If the primary analysis test was significant, subsequent key secondary endpoints (OS in BM-ve Population, PFS by IRC assessment in the ITT Population, OS in the ITT Population) were tested in a sequential manner as shown below, where a given hypothesis was only declared statistically significant if all hypotheses above it in the hierarchy were also statistically significant. Because the study was stopped when 302 of the 315 PFS events had occurred, the 2-sided alpha level was adjusted from 0.05 to 0.0443 based on a Lan-DeMets alpha-spending function approximating O'Brien-Fleming stopping boundaries. This p-value was inherited by the 3 subsequent hierarchical pre-specified secondary outcomes.

The primary analysis of PFS in the BM-ve Population for comparison between SG and the TPC group was performed using a stratified log-rank test stratified by randomization factors as employed in the randomization. Estimate of HR and its 95% confidence interval (CI) was based on stratified Cox proportional-hazards model with treatment group as the only covariate, stratified by the same stratification factors employed in the randomization. PFS was plotted over time using Kaplan-Meier (KM) curves; median PFS and its associated 95% CIs were determined by the Brookmeyer and Crowley method with log-log transformation. Sensitivity analyses were also conducted.

OS and DOR were analyzed by the same method as the primary PFS analysis.

ORR and CBR were analyzed and compared between groups using the Cochran-Mantel-Haenszel method stratified by the stratification factors used in the randomization. Two-sided 95% CIs were calculated by the Clopper-Pearson exact method.

Safety Endpoints:
Descriptive analyses were performed for safety.

SUMMARY – CONCLUSIONS

Efficacy Results:
The primary efficacy endpoint, PFS in the BM-Ve Population, was met. PFS was significantly longer in the SG group compared with the TPC group in the BM-ve Population. Median time to progression or death by IRC assessment in the BM-ve Population was 5.6 months in the SG group and 1.7 months in the TPC group with a difference of approximately 4 months at the median. The hazard ratio for progression or death by IRC assessment in the BM-ve Population was 0.41 (95% CI: 0.323, 0.519) which represents a 59% decrease in the hazard of disease progression or death for the SG group compared with the TPC group. Supportive analyses of PFS by IRC assessment in the ITT Population and by investigator assessment in the BM-ve and ITT Populations confirm the robustness of results for PFS.

OS was significantly longer with SG than TPC in the BM-ve and ITT Populations. The hazard ratio for death was 0.48 (95% CI: 0.383, 0.592) in the BM-ve Population and 0.51 (95% CI: 0.414, 0.624) in the ITT Population, which represent a 52% and 49% decrease in the hazard of death, respectively, for patients in the SG group compared with patients in the TPC group.

ORR by IRC assessment was significantly higher in the SG group than in the TPC group in the BM-ve Population (34.9% versus 4.7%, respectively; $p<0.0001$) and the ITT Population (31.1% versus 4.2%; $p<0.0001$). Similar results were seen for ORR by investigator assessment in the BM-ve and ITT Populations.
The Kaplan-Meier estimate of median DOR was 6.3 months (95% CI: 5.5, 9.0) and 3.6 months in the SG and TPC groups, respectively, by IRC assessment and 7.0 months (95% CI: 5.7, 8.4) and 2.9 months (95% CI: 2.8, 4.2) in the SG and TPC groups, respectively, by investigator assessment.

Sensitivity analyses confirm the robustness of results and subgroup analyses confirm the consistency of results for PFS, OS, and ORR.

Safety Results:

- GI events (nausea and diarrhea), myelosuppression (primarily neutropenia and anemia), fatigue, and alopecia were reported at a higher incidence in the SG group compared with the TPC group.
    - Most of the GI and myelosuppressive events seen with SG were grade 1 or grade 2, nonserious and did not require permanent discontinuation of treatment or either a dose reduction or treatment interruption. These events were managed by routine supportive care, including anti-emetics, anti-propulsives, and immunostimulants.
    - Despite the higher occurrence of neutropenia with SG, few cases were febrile (5.8% and 2.7% in the SG and TPC groups, respectively). However, there was a higher incidence of febrile neutropenia in subjects who were homozygous for the UGTI1A1 *28 allele compared with subjects who had either 1 copy or no copies of the *28 allele (17.6% versus 2.7% and 5.2%, respectively).
    - Additionally, grade 3 or grade 4 infections were infrequent and the incidence of serious infections was similar in the SG and TPC groups (8.1% and 6.7%, respectively).
    - Fatigue and alopecia were also primarily grade 1 or grade 2 and were nonserious events. Only 0.8% and 0.4% of the patients in the SG and TPC groups permanently discontinued treatment because of fatigue.
- No cases of anaphylaxis were seen with SG.
- Fatal AEs within 30 days of the last SG dose were infrequent. Only 1 patient (0.4%) in the SG group (unrelated respiratory failure; unrelated) compared with 3 patients (1.3%) in the TPC group (related neutropenic sepsis and unrelated sepsis and general physical health deterioration) had an AE with a fatal outcome.
- A similar percentage of patients in the SG and TPC groups had at least one SAE (26.7% and 28.1%, respectively). The most common SAEs in the SG group compared with the TPC group were febrile neutropenia (5.0% vs 1.8%), diarrhea (3.5% vs no patients), and pneumonia (2.7% vs 1.8%).
- A similar percentage of patients in the SG and TPC groups (4.7% and 5.4%, respectively) had an AE leading to permanent discontinuation of study drug. The AEs leading to permanent discontinuation of study drug were varied and none occurred in >2 subjects in the SG group.
- AEs leading to a dose reduction occurred in a lower percentage of patients in the SG group compared with the TPC group (21.7% and 26.3%, respectively).
- Diarrhea was the only AE leading to a dose reduction that occurred in a higher (≥2%) percentage of patients in the SG group compared with the TPC group (4.7% and 0.4%, respectively).
- AEs leading to a treatment interruption occurred in a higher percentage of patients in the SG group compared with the TPC group (62.8% and 38.8%, respectively). AEs leading to a treatment interruption that occurred in a higher (≥5%) percentage of patients in the SG group than TPC group were neutropenia (28.3% and 12.1%, respectively), neutrophil count decreased (19.4% and 10.3%, respectively), and diarrhea (5.4% and 0.4%).
- No evidence for liver or kidney injury was seen with SG.

Overall Conclusions:

SG provides a significant benefit over single-agent chemotherapy for heavily pretreated TNBC patients. SG has a manageable safety profile.

Date of the report: 26 Oct 2020

3.1. Protocol Amendments and Description

Protocol Amendment Date No. of Patients Enrolled	Key Changes
Amendment 1 05 May 2017 no patients	Added guidelines for infusion reactions, dose delay, dose reduction and treatment discontinuation Added the inclusion criterion that all patients should have been previously treated with taxane regardless of disease stage (adjuvant, neoadjuvant or advanced) when it was given Revised the inclusion criterion that patients with treated, non-progressive brain metastases must have stable MRI scans for at least 3 months, including within 4 weeks of study entry Added collection of *BRCA1* and *BRCA2* mutational status, if known Removed baseline brain imaging requirement to rule out brain metastases Removed the CTCAE PRO questionnaire
Amendment 2 31 Jul 2017 246 patients	Revised the CT/MRI scans from every 6 weeks for 24 weeks to every 6 weeks for 36 weeks
Amendment 3 22 Feb 2018 no patients	Allowed patients with locally advanced TNBC to be enrolled Sample size increased from 328 to 488 patients Defined as <10% expression for ER and PR and negative for human epidermal growth factor receptor 2 HER2 by in-situ hybridization Added the secondary objective and secondary efficacy endpoint of PFS in the ITT Population Added that ORR and PFS would also be determined by the investigator Added PFS and OS in the ITT Population Added an exploratory analysis of Trop-2 tumor expression and efficacy Increased the sample size and number of participating sites Limited the number of patients with brain metastasis at 15% Added eligibility requirements for patients who had either a contraindication or were intolerant to taxanes Excluded patients who had received >5 prior standard of care chemotherapies for locally advanced or metastatic disease Excluded patients with active chronic inflammatory bowel disease (ulcerative colitis, Crohn disease) and patients with a history of bowel obstruction Excluded patients who had received a live vaccine within 30 days of randomization
Amendment 4 11 May 2018 382 patients	Removed secondary objective and secondary efficacy endpoint of PFS by investigator assessment Added inclusion criteria that defined stable CNS disease for patients with brain metastasis Removed the exclusion of patients who had received >5 prior standard of care chemotherapies for locally advanced or metastatic disease Excluded patients who had previously received irinotecan Excluded patients with rapid deterioration during screening Added a hierarchical testing strategy for efficacy

Protocol Amendment Date No. of Patients Enrolled	Key Changes
Amendment 5 14 June 2019 no patients	Removed assessment of other tumor markers Clarified that both total and free SN-38 would be assessed Added that patients who were receiving clinical benefit from SG at the end of the study would be enrolled in a rollover study to ensure continued access to SG Added that disease progression was not to be reported as an AE Removed the interim futility analysis for PFS Added that the significance level for the final anylsis of OS in the ITT population would be determined by the Lan-DeMets spending function to ensure alpha was controlled at a 2-sided alpha of 0.05[a]
Amendment 6 26 August 2019 220 patients	Clarified PK sampling time points

[a] Subsequently changed to a 2-sided alpha of 0.0443 in a SAP amendment since 302 of the prespecified 315 PFS events was used in the final analysis.
AE=adverse event; BM-ve=brain metastasis negative; CNS=central neverous system; CT=computed tomography; CTCAE=Common Terminology Criteria for Adverse Events; ER=estrogen receptor; HER2=human epidermal growth factor receptor 2; ITT=inten-to-treat; PFS=progression-free survival; ORR=objective response rate; OS=overall survival; PK=pharmacokinetic; PR=progesterone receptor; PRO=Patient-reported Outcome; SAP=Statistical Analysis Plan; SG=sacituzumab govitecan; TNBC=triple-negative breast cancer

3.2. IMMU-132-05: List of Principal Investigators

Principal Investigator	Study Site
PPD	Tennessee Oncology, PLLC 250 25th Avenue North Suite 100 Nashville TN 37203 USA
PPD	Florida Cancer Specialists & Research Institute 551 N Cattlemen Rd Suite 101 Sarasota FL 34232 USA
PPD	Research Medical Center 2340 East Meyer Blvd Kansas City MO 64132 USA
PPD	Center for Cancer and Blood Disorders 800 W Magnolia Ave Fort Worth TX 76104 USA

Principal Investigator	Study Site
PPD	Vanderbilt Breast Center at One Hundred Oaks 719 Thompson Lane Suite 25000 Nashville TN 37204 USA
Aditya Bardia	Massachusetts General Hospital 55 Fruit Street Boston MA 02114 USA
Aditya Bardia	Dana-Farber Cancer Institute 450 Brookline Avenue Boston, MA 02215-5418 USA
PPD	Georgetown University Medical Center 3800 Reservoir Road NW Washington DC 20007 USA
PPD	UF Health Cancer Center at Orlando Health 1400 South Orange Avenue Orlando FL 32806 USA
PPD	The University of Chicago Medical Center 5841 S. Maryland Ave. Chicago IL 60637 USA
PPD	Swedish Cancer Institute 1221 Madison Street Seattle WA 98104 USA
PPD	Tennessee Oncology - Chattanooga Oncology & Hematology Associates 605 Glenwood Dr Suite 200 Chattanooga TN 37404 USA
PPD	University of Colorado Hospital - Anschutz Cancer Pavilion 12648 East 17th Avenue Aurora CO 80045 USA
PPD	Florida Cancer Specialists & Research Institute 1309 North Flagler Drive West Palm Beach FL 33401 USA

Principal Investigator	Study Site
PPD	Columbia University Medical Center 161 Fort Washington Avenue Herbert Irving Pavilion New York NY 10032 USA
PPD	Florida Cancer Specialists & Research Institute- Fort Myers Broadway Office 3840 Broadway Fort Myers FL 33901 USA
PPD	Virginia G. Piper Cancer Center at HonorHealth 800 East 28th Street Suite 602 Minneapolis MN 55407 USA
PPD	Northside Hospital 1835 Savoy Dr Ste 300 Atlanta GA 30341 USA
PPD	Washington University School of Medicine 660 S Euclid Avenue St. Louis MO 63110 USA
PPD	Texas Oncology - Baylor Charles A. Sammons Cancer Center 3535 Worth Street Dallas TX 75246 USA
PPD	Rocky Mountain Cancer Centers 1700 S Potomac Street Aurora CO 80012 USA
PPD	Virginia Cancer Specialists, PC 8503 Arlington Blvd Suite 400 Fairfax VA 22031 USA
PPD	Blue Ridge Cancer Care 1900 Electric Road First Floor Salem VA 24153 USA

Principal Investigator	Study Site
PPD	US Oncology Research Pharmacy 910 East Houston Street Suite 100 Tyler TX 75702 USA
PPD	Virginia Oncology Associates, P.C. 5900 Lake Wright Drive Suite 300 Norfolk VA 23502 USA
PPD	Texas Oncology-Denton 2600 Scripture Street Denton TX 76210 USA
PPD	Texas Oncology-Plano East 3705 W. 15th Street Plano TX 75075-7787 USA
PPD	Miami Cancer Institute – Baptist Health South Florida 8900 North Kendall Drive Miami FL 33176 USA
PPD	Illinois Cancer Specialists 880 W. Central Road Suite 8200 Arlington Heights IL 60005 USA
PPD	University of Kansas Cancer Center - The Richard and Annette Bloch Cancer Care Pavilion 2330 Shawnee Mission Parkway Westwood KS 66205-2005 USA
Aditya Bardia	Beth Israel Deaconess Medical Center (BIDMC) 330 Brookline Avenue Boston MA 02215-5400 USA
PPD	University of Pittsburgh Cancer Institute 300 Halket Street Pittsburgh PA 15213 USA
PPD	Methodist Hospital 6550 Fannin Street SM1661 Houston TX 77030 USA

Principal Investigator	Study Site
PPD	University of California, San Francisco (UCSF) - Innovation, Technology & Alliances 1825 4th Street San Francisco CA 94158 USA
PPD	UCLA Jonsson Comprehensive Cancer Center 2020 Santa Monica Boulevard Suite 600 Santa Monica CA 90404 USA
PPD	Mayo Clinic Cancer Center (MCCC) - Rochester 200 First Street SW Rochester MN 55905 USA
PPD	Providence Medical Group 4805 NE Glisan Street Portland OR 97213 USA
PPD	Southern Cancer Center 29653 Anchor Cross Blvd Mobile AL 36526 USA
PPD	Maryland Oncology Hematology, PA- Clinton 7704 Matapeake Business Drive Suite 200 Brandywine MD 20613 USA
PPD	New York Oncology Hematology, PC 400 Patroon Creek Boulevard Suite 1 Albany NY 12206 USA
PPD	Memorial Sloan-Kettering Cancer Center 1275 York Ave New York NY 10065 USA
PPD	Norwalk Hospital 34 Maple Street Norwalk CT 06856 USA

Principal Investigator	Study Site
PPD	UNC Hospitals, The University of North Carolina at Chapel Hill 101 Manning Drive Chapel Hill NC 27599-7600 USA
PPD	University Cancer & Blood Center, LLC 3320 Old Jefferson Road Building 700 Athens GA 30607 USA
PPD	The Ohio State University Wexner Medical Center James Cancer Hospital 460 W 10th Avenue Columbus OH 43210 USA
PPD	Sylvester Comprehensive Cancer Center 1475 N.W. 12th Avenue Miami FL 33136 USA
PPD	North Shore Hematology Oncology Associates DBA NY Cancer and Blood Specialist 1201 Rte.112 Suite 350 Port Jefferson NY 11776 USA
PPD	Allegheny General Hospital 320 East North Avenue Pittsburgh PA 15212 USA
PPD	The West Clinic, P.C. d/b/a West Cancer CenterWest Cancer Center 7945 Wolf River Blvd Germantown TN 38138 USA
PPD	Rutgers Cancer Institute of New Jersey 195 Little Albany Street New Brunswick NJ 08903 USA
Aditya Bardia	Massachusetts General Hospital 55 Fruit Street Boston MA 02114 USA

Principal Investigator	Study Site
PPD	Jewish General Hospital 3755 Côte-Sainte-Catherine Montreal QC H3T 1E2 Canada
PPD	Cross Cancer Institute 11560 University Avenue Edmonton AB T6G 1Z2 Canada
PPD	Nova Scotia Cancer Center 5820 University Avenue Halifax NS B3H 1V7 Canada
PPD	Clinique Sainte-Elisabeth Place Louise Godin 15 Namur 5000 Belgium
PPD	Universitaire Ziekenhuizen Leuven Herestraat 49 Leuven 3000 Belgium
PPD	Institut Jules Bordet Rue Héger-Bordet 1 Bruxelles 1000 Belgium
PPD	Universitair Ziekenhuis Brussel Laarbeeklaan 101 Brussel 1090 Belgium
PPD	Institut Curie 26 Rue d'Ulm Paris 75005 France
PPD	Institut de Cancerologie de l'Ouest- Centre Rene Gauducheau Rue Moise-Marcinhes 7 Meyrin-Geneva 1217 France
PPD	Centre Eugène Marquis Service d'Oncologie Medicale Rue de la Bataille Flandres Dunkerque CS44229 Rennes Cedex 35042 France

Principal Investigator	Study Site
PPD	Institut Gustave Roussy Service d'Oncologie 114 Rue Edouard Vaillant Villejuif 94800 France
PPD	Centre Léon Bérard 28 rue Laënnec Lyon 69008 France
PPD	Institut Curie - Hopital-René-Huguenin 35, rue Dailly Saint-Cloud 92210 France
PPD	ICM Vald'Aurelle 208 rue des Apothicaires Montpellier Cedex 5 34298 France
PPD	CHU de Besançon 3 Boulevard Fleming Besançon Cedex 25030 France
PPD	Institut Claudius Regaud- IUTC-O 1 avenue Irène Joliot Curie Touluse Cedex 9 31059 France
PPD	Institut de Cancerologie de l'Ouest - Centre Paul Papin 15 rue André Boquel-CS 10059 Angers Cedex 2 49055 France
PPD	Hospital Universitario Ramón y Cajal Ctra. De Colmenar Viejo, Km. 9,100 Madrid Madrid 28034 Spain
PPD	Hospital Teresa Herrera Materno-Infantil-CHUAC As Xubias, 84 A Coruña 15006 Spain
PPD	Hospital Universitario Vall d'Hebron Passeig de la Vall d'Hebron, 119-129 Barcelona 08035 Spain

Principal Investigator	Study Site
PPD	Hospital del Mar Passeig Maritim, 25-29 Barcelona 08003 Spain
PPD	Institut Catala d'Oncologia Hospitalet Av. Gran Via de L'hospitalet, 199-203 L'Hospitalet de Llobregat 08908 Spain
PPD	Hospital Universitario 12 de Octubre Avenida de Córdoba S/N Madrid Madrid 28041 Spain
PPD	Hospital Universitario Virgen del Rocío Avenida de Manuel Siurot s/n Sevilla Sevilla 410013 Spain
PPD	Hospital Quirón Barcelona Plaza Alfonso Comí 5-7 Barcelona Barcelona 08023 Spain
PPD	Complejo Hospitalario Universitario de Santiago (CHUS) Travesía de la Choupera, s/n Santiago de Compostela A Coruna 15706 Spain
PPD	The Royal Surrey County Hospital NHS Foundation Trust Egerton Road Guildford GU2 7XX UK
PPD	The Royal Free London NHS Foundation Trust - The Royal Free Hospital Pond Street London NW3 2QG UK
PPD	The Christie NHS Foundation Trust Wilmslow Road Manchester M20 4BX UK
PPD	University Hospital Coventry and Warwickshire NHS Trust - The Arden Centre Clifford Bridge Road Coventry CV2 2DX UK

Principal Investigator	Study Site
PPD	Taunton and Somerset NHS Foundation Trust – Musgrove Park Hospital Parkfield Drive Taunton TA1 5DA UK
PPD	Barts Health NHS Trust-St Bartholomew's Hospital West Smithfield London EC1A 7BE UK
PPD	Institut für Versorgungsforschung in der Onkologie Neversstrasse 5 Koblenz 56068 Germany
PPD	Facharztzentrum Eppendorf Eppendorfer Landstrasse 42 Hamburg 20249 Germany