Clinical trial results:
A double-blind, randomized, placebo-controlled, Phase I/II Study evaluating the safety, immunogenicity and clinical activity of neoadjuvant treatment with WT1-A10 + AS15 Antigen-Specific Cancer Immunotherapeutic in combination with standard therapy in patients with WT1-positive Stage II or III breast cancer.

Summary

EudraCT number	2010-019909-42
Trial protocol	BE DE GB DK
Global end of trial date	14 November 2014
Results information	
Result version number	v2 (current)
This version publication date	20 June 2021
First version publication date	05 March 2016
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification	
Sponsor protocol code	113172
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01220128
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 November 2014
Global end of trial reached?	Yes
Global end of trial date	14 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study was conducted in 2 consecutive segments with specific objectives:
Phase I Segment
-Objectives concerning cohorts A, B, C and D: To evaluate the safety and immunogenicity of WT1 ASCI administration in combination with standard treatment.
Phase II Segment
-To further assess the safety, immunogenicity and the clinical activity of WT1 ASCI in combination with standard treatment per group and in the overall population (i.e., including the patients enrolled during the Phase I segment of the study).

Protection of trial subjects:

The vaccine/placebo recipients were to be observed closely for at least 30 minutes with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccine(s)/product(s).
For patients in Cohort B and C, the study product administration had to be done at least 60 minutes prior to administration of chemotherapy. The patient was observed closely for at least 30 minutes following the administration of the study product with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	11 April 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	66
EEA total number of subjects	55

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	40
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Out of the 66 enrolled patients, 6 patients did not receive study product doses and were hence excluded prior to study start.

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

Double-blind, randomized, placebo-controlled study including 2 segments, a Phase I segment and a Phase II segment. The Phase I segment was a randomized (2:1), double-blinded, placebo-controlled study for cohorts A, B and C and an open label, single treatment schedule study for Cohort D. The Phase II segment was a randomized (2:1), double-blinded, placebo-controlled study for cohorts A, B, C, and E.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A-WT1 Group

Arm description:

This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy, concurrently with administration of WT1 ASCI according to the treatment schedule.

Arm type	Experimental
Investigational medicinal product name	WT1-A10 + AS15
Investigational medicinal product code	WT1-A10 + AS15
Other name	WT1 ASCI - GSK2302024A
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 6 or 8 injections at 3 weeks apart of WT1 ASCI, injected intramuscularly in the deltoid or lateral region of the thigh.

Investigational medicinal product name	Aromatase inhibitor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

This treatment consisted of any aromatase inhibitor (e.g. letrozole or exemestane), administered intravenously in Cohort A Groups daily for either 18 (if 6 doses of WT1 ASCI/placebo) or 24 weeks (if 8 doses of WT1 ASCI/placebo).

Arm title	Cohort A-Placebo Group

Arm description:

This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy, concurrently with administration of placebo, according to the treatment schedule.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 6 or 8 doses at 3 weeks apart of placebo (sucrose/mannitol-based formulation reconstituted with an oil-in-water emulsion), injected intramuscularly in the deltoid or lateral region of the thigh.

Investigational medicinal product name	Aromatase inhibitor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

This treatment consisted of any aromatase inhibitor (e.g. letrozole or exemestane), administered intravenously in Cohort A Groups daily for either 18 (if 6 doses of WT1 ASCI/placebo) or 24 weeks (if 8 doses of WT1 ASCI/placebo).

Arm title	Cohort B-WT1 Group

Arm description:

This group included breast cancer patients who received WT1 ASCI, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel, according to the treatment schedule.

Arm type	Experimental
Investigational medicinal product name	WT1-A10 + AS15
Investigational medicinal product code	WT1-A10 + AS15
Other name	WT1 ASCI
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 6 or 8 injections at 3 weeks apart of WT1 ASCI, injected intramuscularly in the deltoid or lateral region of the thigh.

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses at 3 weeks apart, and for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses in Cohort C Groups and 6 doses 3 weeks apart in Cohort B and D Groups, while for the 8 WT1 ASCI-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/placebo-dose schedule 3 or 6 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 6 doses 3 weeks apart (Cohort C patients with this schedule did not receive this treatment), while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Groups, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: only in the 8 WT1 ASCI/Placebo-dose schedule patients received 4 at 3 weeks apart or 12 weekly doses. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Arm title	Cohort B-Placebo Group

Arm description:

This group included breast cancer patients who received placebo, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intraventricular use

Dosage and administration details:

Subjects received 6 or 8 doses at 3 weeks apart of Placebo (sucrose/mannitol-based formulation reconstituted with an oil-in-water emulsion), injected intramuscularly in the deltoid or lateral region of

the thigh.

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses at 3 weeks apart, and for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses in Cohort C Groups and 6 doses 3 weeks apart in Cohort B and D Groups, while for the 8 WT1 ASCI-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/placebo-dose schedule 3 or 6 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 6 doses 3 weeks apart (Cohort C patients with this schedule did not receive this treatment), while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Groups, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: only in the 8 WT1 ASCI/Placebo-dose schedule patients received 4 at 3 weeks apart or 12 weekly doses. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Arm title	Cohort C-WT1 Group

Arm description:

This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of WT1-ASCI, 5-Fluorouracil, Carboplatin, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Arm type	Experimental
Investigational medicinal product name	WT1-A10 + AS15
Investigational medicinal product code	WT1-A10 + AS15
Other name	WT1 ASCI
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 6 or 8 injections at 3 weeks apart of WT1-ASCI, injected intramuscularly in the deltoid or lateral region of the thigh .

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort C Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 or 6 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. The administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle).

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort C Groups in 6 doses at 3 weeks apart, on the same day as WT1 ASCI/placebo administration (Day 1 of each cycle).

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses at 3 weeks apart, and for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses in Cohort C Groups and 6 doses 3 weeks apart in Cohort B and D Groups, while for the 8 WT1 ASCI-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/placebo-dose schedule 3 or 6 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 6 doses 3 weeks apart (Cohort C patients with this schedule did not receive this treatment), while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Groups, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: only in the 8 WT1 ASCI/Placebo-dose schedule patients received 4 at 3 weeks apart or 12 weekly doses. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Arm title	Cohort C-Placebo Group

Arm description:

This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing

breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of placebo, 5-Fluorouracil, Carboplatin AUC, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 6 or 8 doses at 3 weeks apart of Placebo (sucrose/mannitol-based formulation reconstituted with an oil-in-water emulsion), injected intramuscularly in the deltoid or lateral region of the thigh.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort C Groups in 6 doses at 3 weeks apart, on the same day as WT1 ASCI/placebo administration (Day 1 of each cycle).

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort C Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 or 6 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. The administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle).

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses at 3 weeks apart, and for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses in Cohort C Groups and 6 doses 3 weeks apart in Cohort B and D Groups, while for the 8 WT1 ASCI-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/placebo-dose schedule 3 or 6 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 6 doses 3 weeks apart (Cohort C patients with this schedule did not receive this treatment), while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Groups, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: only in the 8 WT1 ASCI/Placebo-dose schedule patients received 4 at 3 weeks apart or 12 weekly doses. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Arm title	Cohort D-WT1-D14 Group

Arm description:

This group included patients with hormone receptor-positive and HER2 non-overexpressing breast cancer, who received WT1 ASCI, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Arm type	Experimental
Investigational medicinal product name	WT1-A10 + AS15
Investigational medicinal product code	WT1-A10 + AS15
Other name	WT1 ASCI
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 6 or 8 injections at 3 weeks apart, of WT1 ASCI injected intramuscularly in the deltoid or lateral region of the thigh .

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses at 3 weeks apart, and for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses in Cohort C Groups and 6 doses 3 weeks apart in Cohort B and D Groups, while for the 8 WT1 ASCI-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/placebo-dose schedule 3 or 6 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 6 doses 3 weeks apart (Cohort C patients with this schedule did not receive this treatment), while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: for the 6 WT1 ASCI/Placebo-dose schedule 3 doses 3 weeks apart, while for the 8 WT1 ASCI/Placebo-dose schedule 4 doses at 3 weeks apart. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Groups, the administration was on Day 14 of each cycle.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously in Cohort B, C and D Groups: only in the 8 WT1 ASCI/Placebo-dose schedule patients received 4 at 3 weeks apart or 12 weekly doses. For Cohort B and C Groups, the administration was on the same day as the administration of WT1 ASCI/placebo (Day 1 of each cycle). For Cohort D Group, the administration was on Day 14 of each cycle.

Number of subjects in period 1[1]	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group
Started	15	7	9
Completed	11	6	6
Not completed	4	1	3
Adverse event, serious fatal	2	-	-
Consent withdrawn by subject	1	-	-
Sponsor study termination	-	1	-
Adverse event, non-fatal	1	-	-
Unspecified	-	-	1
Progressive disease	-	-	2

Number of subjects in period 1[1]	Cohort B-Placebo Group	Cohort C-WT1 Group	Cohort C-Placebo Group
Started	6	11	4
Completed	6	11	4
Not completed	0	0	0
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	-	-
Sponsor study termination	-	-	-
Adverse event, non-fatal	-	-	-
Unspecified	-	-	-
Progressive disease	-	-	-

Number of subjects in period 1[1]	Cohort D-WT1-D14 Group
Started	8
Completed	3
Not completed	5
Adverse event, serious fatal	1
Consent withdrawn by subject	-
Sponsor study termination	1
Adverse event, non-fatal	3
Unspecified	-

Progressive disease	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of the 66 enrolled patients, 6 patients did not receive study product doses and were hence excluded prior to study start.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A-WT1 Group
Reporting group description:	
This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy, concurrently with administration of WT1 ASCI according to the treatment schedule.	
Reporting group title	Cohort A-Placebo Group
Reporting group description:	
This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy, concurrently with administration of placebo, according to the treatment schedule.	
Reporting group title	Cohort B-WT1 Group
Reporting group description:	
This group included breast cancer patients who received WT1 ASCI, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel, according to the treatment schedule.	
Reporting group title	Cohort B-Placebo Group
Reporting group description:	
This group included breast cancer patients who received placebo, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	
Reporting group title	Cohort C-WT1 Group
Reporting group description:	
This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of WT1-ASCI, 5-Fluorouracil, Carboplatin, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	
Reporting group title	Cohort C-Placebo Group
Reporting group description:	
This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of placebo, 5-Fluorouracil, Carboplatin AUC, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	
Reporting group title	Cohort D-WT1-D14 Group
Reporting group description:	
This group included patients with hormone receptor-positive and HER2 non-overexpressing breast cancer, who received WT1 ASCI, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	

Reporting group values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group
Number of subjects	15	7	9
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			

85 years and over			

Age continuous			
Units: years			
arithmetic mean	69.3	70.9	49.3
standard deviation	± 10.4	± 7.1	± 15.6
Gender categorical			
Units: Subjects			
Female	15	7	9
Male	0	0	0

Reporting group values	Cohort B-Placebo Group	Cohort C-WT1 Group	Cohort C-Placebo Group
Number of subjects	6	11	4
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	60.7	52.9	53.3
standard deviation	± 9.8	± 10.6	± 6.2
Gender categorical			
Units: Subjects			
Female	6	11	4
Male	0	0	0

Reporting group values	Cohort D-WT1-D14 Group	Total	
Number of subjects	8	60	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	

Age continuous Units: years			
arithmetic mean	49.6		
standard deviation	± 8.7	-	
Gender categorical Units: Subjects			
Female	8	60	
Male	0	0	

End points

End points reporting groups

Reporting group title	Cohort A-WT1 Group
Reporting group description:	
This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy, concurrently with administration of WT1 ASCI according to the treatment schedule.	
Reporting group title	Cohort A-Placebo Group
Reporting group description:	
This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy, concurrently with administration of placebo, according to the treatment schedule.	
Reporting group title	Cohort B-WT1 Group
Reporting group description:	
This group included breast cancer patients who received WT1 ASCI, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel, according to the treatment schedule.	
Reporting group title	Cohort B-Placebo Group
Reporting group description:	
This group included breast cancer patients who received placebo, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	
Reporting group title	Cohort C-WT1 Group
Reporting group description:	
This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of WT1-ASCI, 5-Fluorouracil, Carboplatin, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	
Reporting group title	Cohort C-Placebo Group
Reporting group description:	
This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of placebo, 5-Fluorouracil, Carboplatin AUC, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	
Reporting group title	Cohort D-WT1-D14 Group
Reporting group description:	
This group included patients with hormone receptor-positive and HER2 non-overexpressing breast cancer, who received WT1 ASCI, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.	

Primary: Number of subjects with severe toxicities

End point title	Number of subjects with severe toxicities[1]
End point description:	
Severe toxicity was defined as follows: − A Grade 3 or higher toxicity that is related or possibly related to the combined administration of standard treatment and GSK2302024A/placebo − A decrease in Left Ventricular Ejection Fraction (LVEF) from baseline with ≥ 10 points and at < 50% that is related or possibly related to the combined administration of treatment and that is confirmed by a second LVEF assessment within approximately 3 weeks. − A Grade 2 or higher cardiac ischemia/infarction that is related or possibly related to the combined administration of standard treatment and GSK2302024A /placebo. − A Grade 2 or higher allergic reaction occurring within 24 hours following the administration. − A Grade 3 or higher blood/bone marrow toxicity that was considered as related or possibly related to the combined Administration. − A decrease in renal function at the time of administration that was considered as related or possibly related.	
End point type	Primary
End point timeframe:	
From Week 0 to Week 26/32 (period starting from WT1 ASCI/placebo treatment allocation and ending	

with the concluding Visit i.e.: Week 26 for patients receiving 6 injections and Week 32 for patients receiving 8 injections)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Any severe toxicity	0	0	1	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Any severe toxicity	1	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with an anti-WT1 humoral response

End point title	Number of patients with an anti-WT1 humoral response[2]

End point description:

For initially seronegative patients: post-administration antibody concentration ≥ 9 EU/mL
For initially seropositive patients: post-administration antibody concentration ≥ 2 fold the pre-administration antibody concentration.

End point type	Primary

End point timeframe:

At post-WT1 ASCI/placebo Dose 4 (Week 13)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	4	8	6
Units: Subjects				
Anti-WT1 response	10	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	3	3	
Units: Subjects				
Anti-WT1 response	6	0	2	

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with adverse events (AEs)

End point title	Number of patients with adverse events (AEs)[3]

End point description:

An AE is any untoward medical occurrence in a clinical investigation patient, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.
An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product.
For marketed medicinal products, this also includes failure to produce expected benefits (i.e., lack of efficacy), abuse or misuse.

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Any AE(s)	15	5	9	6

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Any AE(s)	11	4	7	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events SAE(s)

End point title	Number of subjects with serious adverse events SAE(s)[4]

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of hospitalization, causes disability/incapacity or is a congenital anomaly/birth defect in the offspring of a study patient.
In this study, an event which was part of the natural course of the disease under study (i.e., disease progression/recurrence) was captured in the study/as an efficacy measure. Therefore it was not reported as an SAE. Progression/recurrence of the tumor was recorded in the clinical assessments in the electronic case report form (eCRF). Death due to progressive disease was recorded on a specific form in the eCRF but not as an SAE.

End point type	Primary

End point timeframe:

From Week 0 to Week 26/32 (period starting from WT1 ASCI/placebo treatment allocation and ending with the concluding Visit i.e.: Week 26 for patients receiving 6 injections and Week 32 for patients receiving 8 injections)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Any SAE(s)	3	0	4	2

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Any SAE(s)	5	1	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with alanine aminotransferase increased abnormality, by CTCAE maximum grade

End point title	Number of subjects with alanine aminotransferase increased abnormality, by CTCAE maximum grade[5]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5)

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	12	5	8	4
Grade 1	2	1	1	2
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	1	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	6	2	1	
Grade 1	5	2	2	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with alkaline phosphatase increased abnormality, by CTCAE maximum grade

End point title	Number of subjects with alkaline phosphatase increased abnormality, by CTCAE maximum grade[6]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	10	5	8	6
Grade 1	5	1	1	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	7	3	1	
Grade 1	4	1	2	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anemia, by CTCAE maximum grade

End point title	Number of subjects with anemia, by CTCAE maximum grade[7]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	12	7	1	0
Grade 1	2	0	7	4
Grade 2	1	0	0	0
Grade 3	0	0	1	0
Grade 4	0	0	0	0
Grade Unknown	0	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	0	0	2	
Grade 1	7	3	2	
Grade 2	4	1	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with aspartate aminotransferase increased abnormality, by CTCAE maximum grade

End point title	Number of subjects with aspartate aminotransferase increased abnormality, by CTCAE maximum grade[8]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	12	4	8	6
Grade 1	3	2	1	0
Grade 2	1	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	7	1	2	
Grade 1	4	3	1	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with blood bilirubin increased abnormality, by CTCAE maximum grade

End point title	Number of subjects with blood bilirubin increased abnormality, by CTCAE maximum grade[9]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	15	5	9	6
Grade 1	0	1	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	11	2	3	
Grade 1	0	0	0	
Grade 2	0	1	0	
Grade 3	0	1	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with creatine increased abnormality, by CTCAE maximum grade

End point title	Number of subjects with creatine increased abnormality, by CTCAE maximum grade[10]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	11	4	8	5
Grade 1	4	2	1	1
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	4	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	10	3	3	
Grade 1	1	1	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hemoglobin increased abnormality, by CTCAE maximum grade

End point title	Number of subjects with hemoglobin increased abnormality, by CTCAE maximum grade[11]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	15	6	9	6
Grade 1	0	1	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	11	4	4	
Grade 1	0	0	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hypercalcemia abnormality, by CTCAE maximum grade

End point title	Number of subjects with hypercalcemia abnormality, by CTCAE maximum grade[12]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	14	3	8	6
Grade 1	1	3	1	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	3	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	11	4	3	
Grade 1	0	0	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hyperkalemia abnormality, by CTCAE maximum grade

End point title	Number of subjects with hyperkalemia abnormality, by CTCAE maximum grade[13]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	15	5	7	6
Grade 1	0	1	1	0
Grade 2	0	0	1	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	10	4	3	
Grade 1	1	0	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hypernatremia abnormality, by CTCAE maximum grade

End point title	Number of subjects with hypernatremia abnormality, by CTCAE maximum grade[14]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	14	4	9	6
Grade 1	1	2	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	10	4	3	
Grade 1	0	0	0	
Grade 2	1	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hypoalbuminemia abnormality, by CTCAE maximum grade

End point title	Number of subjects with hypoalbuminemia abnormality, by CTCAE maximum grade[15]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	13	6	9	5
Grade 1	1	0	0	1
Grade 2	1	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	9	3	3	
Grade 1	2	1	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hypocalcemia abnormality, by CTCAE maximum grade

End point title	Number of subjects with hypocalcemia abnormality, by CTCAE maximum grade[16]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	12	6	5	4
Grade 1	3	0	3	1
Grade 2	0	0	1	1
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	10	3	3	
Grade 1	1	1	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hypokalemia abnormality, by CTCAE maximum grade

End point title	Number of subjects with hypokalemia abnormality, by CTCAE maximum grade[17]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	15	6	9	6
Grade 1	0	0	0	0
Grade 2	0	0	1	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	10	4	3	
Grade 1	1	0	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hyponatremia abnormality, by CTCAE maximum grade

End point title	Number of subjects with hyponatremia abnormality, by CTCAE maximum grade[18]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and post 30 days post last administration

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	15	6	5	6
Grade 1	0	0	4	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	1	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	11	4	3	
Grade 1	0	0	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with lymphocyte count decreased abnormality, by CTCAE maximum grade

End point title	Number of subjects with lymphocyte count decreased abnormality, by CTCAE maximum grade[19]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	9	4	0	0
Grade 1	5	2	3	2
Grade 2	1	1	5	2
Grade 3	0	0	1	2
Grade 4	0	0	0	0
Grade Unknown	0	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	2	1	1	
Grade 1	3	1	1	
Grade 2	5	1	2	
Grade 3	1	1	0	
Grade 4	0	0	0	
Grade Unknown	0	0	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with lymphocyte count increased abnormality, by CTCAE maximum grade

End point title	Number of subjects with lymphocyte count increased abnormality, by CTCAE maximum grade[20]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	15	7	9	6
Grade 1	0	0	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	11	4	4	
Grade 1	0	0	0	
Grade 2	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with neutrophil count decreased abnormality, by CTCAE maximum grade

End point title	Number of subjects with neutrophil count decreased abnormality, by CTCAE maximum grade[21]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	12	6	7	5
Grade 1	3	0	1	1
Grade 2	0	1	1	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	10	3	0	
Grade 1	1	0	0	
Grade 2	0	0	1	
Grade 3	0	1	0	
Grade 4	0	0	3	
Grade Unknown	0	0	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with platelet count decreased abnormality, by CTCAE maximum grade

End point title	Number of subjects with platelet count decreased abnormality, by CTCAE maximum grade[22]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	14	6	8	5
Grade 1	1	1	1	1
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	5	2	2	
Grade 1	5	2	2	
Grade 2	1	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade Unknown	0	0	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with white blood cell decreased abnormality, by CTCAE maximum grade

End point title	Number of subjects with white blood cell decreased abnormality, by CTCAE maximum grade[23]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Grade 0	13	7	6	3
Grade 1	2	0	2	2
Grade 2	0	0	1	1
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade Unknown	0	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Grade 0	7	2	0	
Grade 1	4	1	1	
Grade 2	0	1	0	
Grade 3	0	0	3	
Grade 4	0	0	0	
Grade Unknown	0	0	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with adverse events (AEs), by CTCAE maximum grade reported

End point title	Number of patients with adverse events (AEs), by CTCAE maximum grade reported[24]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Any AE(s) Grade 1	6	1	0	0
Any AE(s) Grade 2	6	4	6	0
Any AE(s) Grade 3	3	0	0	5
Any AE(s) Grade 4	0	0	2	1
Any AE(s) Grade 5	0	0	1	0
Any AE(s)	15	5	9	6

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Any AE(s) Grade 1	0	0	0	
Any AE(s) Grade 2	4	3	2	
Any AE(s) Grade 3	3	0	1	
Any AE(s) Grade 4	4	1	4	
Any AE(s) Grade 5	0	0	0	
Any AE(s)	11	4	7	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events (SAEs), by CTCAE maximum grade reported

End point title	Number of subjects with serious adverse events (SAEs), by CTCAE maximum grade reported[25]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Any SAE(s) Grade 1	0	0	0	0
Any SAE(s) Grade 2	1	0	1	0
Any SAE(s) Grade 3	2	0	0	1
Any SAE(s) Grade 4	0	0	2	1
Any SAE(s) Grade 5	0	0	1	0
Any SAE(s)	3	0	4	2

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Any SAE(s) Grade 1	0	0	0	
Any SAE(s) Grade 2	0	0	0	
Any SAE(s) Grade 3	1	0	1	
Any SAE(s) Grade 4	4	1	4	
Any SAE(s) Grade 5	0	0	0	
Any SAE(s)	5	1	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with adverse events (AEs) assessed by the investigators as causally related to WT1 ASCI treatment, by CTCAE maximum grade reported

End point title	Number of subjects with adverse events (AEs) assessed by the investigators as causally related to WT1 ASCI treatment, by CTCAE maximum grade reported[26]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Any related AE(s) Grade 1	7	2	0	0
Any related AE(s) Grade 2	4	0	3	0
Any related AE(s) Grade 3	1	0	0	0
Any related AE(s) Grade 4	0	0	0	0
Any related AE(s) Grade 5	0	0	0	0
Any related AE(s)	12	2	3	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Any related AE(s) Grade 1	5	0	2	
Any related AE(s) Grade 2	1	1	4	
Any related AE(s) Grade 3	1	0	0	
Any related AE(s) Grade 4	0	0	0	
Any related AE(s) Grade 5	0	0	0	
Any related AE(s)	7	1	6	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events (SAEs), assessed by the investigators as causally related to WT1 ASCI treatment, by CTCAE maximum grade reported

End point title	Number of subjects with serious adverse events (SAEs), assessed by the investigators as causally related to WT1 ASCI treatment, by CTCAE maximum grade reported[27]

End point description:

Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009. Grades refer to the severity of the AE: mild (grade 1), moderate (grade 2), severe or medically significant (grade 3), life-threatening (grade 4) and death (grade 5).

End point type	Primary

End point timeframe:

During the treatment period and up to 30 days post last administration

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	7	9	6
Units: Subjects				
Any related SAE(s) Grade 1	0	0	0	0
Any related SAE(s) Grade 2	1	0	0	0
Any related SAE(s) Grade 3	0	0	0	0
Any related SAE(s) Grade 4	0	0	0	0
Any related SAE(s) Grade 5	0	0	0	0
Any related SAE(s)	1	0	0	0

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	8	
Units: Subjects				
Any related SAE(s) Grade 1	0	0	0	
Any related SAE(s) Grade 2	0	0	0	
Any related SAE(s) Grade 3	1	0	0	
Any related SAE(s) Grade 4	0	0	0	
Any related SAE(s) Grade 5	0	0	0	
Any related SAE(s)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with breast cancer pathological response

End point title	Number of subjects with breast cancer pathological response[28]

End point description:

The pathological response in lymph nodes was evaluated by presence or absence of tumor cells by histopathological examination. Partial responses mark the disappearance of tumor cells, with only small clusters or dispersed cells remaining (more than 90% loss) while complete response indicate no identifiable malignant cells. However, ductal carcinoma in situ may be present.

End point type	Primary

End point timeframe:

During the treatment period, up to Week 26/32

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group	Cohort B-Placebo Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	6	9	6
Units: Subjects				
Partial respose	4	3	5	3
Complete response	0	0	0	2

End point values	Cohort C-WT1 Group	Cohort C-Placebo Group	Cohort D-WT1-D14 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	4	4	
Units: Subjects				
Partial respose	3	1	3	
Complete response	6	3	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were reported during the treatment period and up to 30 days post last administration. SAEs during the entire study period (Week 0 to Week 26/32).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Cohort A-WT1 Group

Reporting group description:

This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy concurrently with administration of WT1 ASCI according to treatment schedule.

Reporting group title	Cohort A-Placebo Group

Reporting group description:

This group included postmenopausal patients with hormone receptor-positive breast cancer who received aromatase inhibitor (AI) as neoadjuvant therapy concurrently with administration of placebo, according to the treatment schedule.

Reporting group title	Cohort B-WT1 Group

Reporting group description:

This group included breast cancer patients who received WT1-ASCI, Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel, according to the treatment schedule.

Reporting group title	Cohort B-Placebo Group

Reporting group description:

This group included breast cancer patients who received placebo, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Reporting group title	Cohort C-WT1 Group

Reporting group description:

This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of WT1-ASCI, 5-Fluorouracil, Carboplatin, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Reporting group title	Cohort C-Placebo Group

Reporting group description:

This group included patients with Human Epidermal Growth Factor Receptor 2 (HER2)-overexpressing breast cancer who received neoadjuvant trastuzumab (Herceptin) therapy, concurrently with administration of placebo, 5-Fluorouracil, Carboplatin, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Reporting group title	Cohort D-WT1-D14 Group

Reporting group description:

This group included patients with hormone receptor-positive and HER2 non-overexpressing breast cancer, who received WT1-ASCI, 5-Fluorouracil, Cyclophosphamide, Docetaxel, Doxorubicin, Epirubicin and Paclitaxel according to the treatment schedule.

Serious adverse events	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 15 (20.00%)	0 / 7 (0.00%)	4 / 9 (44.44%)
number of deaths (all causes)	0	0	1

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cancer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polymyalgia rheumatica			
subjects affected / exposed	1 / 15 (6.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort B-Placebo Group	Cohort C-WT1 Group	Cohort C-Placebo Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	5 / 11 (45.45%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 11 (36.36%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 11 (9.09%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 11 (9.09%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			

subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 11 (9.09%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 11 (9.09%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polymyalgia rheumatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 11 (9.09%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort D-WT1-D14 Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cancer			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			

subjects affected / exposed	2 / 8 (25.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Death				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vestibular disorder				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoidal haemorrhage				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 8 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Vomiting			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Polymyalgia rheumatica			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cohort A-WT1 Group	Cohort A-Placebo Group	Cohort B-WT1 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	5 / 7 (71.43%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Bowen's disease			
subjects affected / exposed	0 / 15 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	2
Flushing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 15 (20.00%)	1 / 7 (14.29%)	8 / 9 (88.89%)
occurrences (all)	3	1	8
Injection site pain			
subjects affected / exposed	4 / 15 (26.67%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Injection site erythema			
subjects affected / exposed	5 / 15 (33.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	5	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Injection site reaction			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	2	0	2
Injection site swelling			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Chills			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0

Injection site discomfort			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Injection site haematoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 15 (33.33%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	5	1	1
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 15 (0.00%)	1 / 7 (14.29%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
Dysgeusia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Neuropathy peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	6 / 9 (66.67%)
occurrences (all)	2	0	6
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Stomatitis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	3
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	4 / 9 (44.44%)
occurrences (all)	0	0	4
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 15 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	9 / 9 (100.00%)
occurrences (all)	0	0	9
Dry skin			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 15 (20.00%)	2 / 7 (28.57%)	2 / 9 (22.22%)
occurrences (all)	3	2	2
Myalgia			

subjects affected / exposed	4 / 15 (26.67%)	0 / 7 (0.00%)	4 / 9 (44.44%)
occurrences (all)	4	0	4
Bone pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	3 / 9 (33.33%)
occurrences (all)	2	0	3
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 15 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 15 (13.33%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Cohort B-Placebo Group	Cohort C-WT1 Group	Cohort C-Placebo Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	11 / 11 (100.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Bowen's disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 6 (66.67%)	7 / 11 (63.64%)	4 / 4 (100.00%)
occurrences (all)	4	7	4
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)	4 / 11 (36.36%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)	3 / 11 (27.27%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	3 / 11 (27.27%)	2 / 4 (50.00%)
occurrences (all)	0	3	2
Injection site reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site swelling			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Injection site discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 6 (33.33%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	3 / 11 (27.27%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 6 (0.00%)	5 / 11 (45.45%)	2 / 4 (50.00%)
occurrences (all)	0	5	2
Dysgeusia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 6 (33.33%)	4 / 11 (36.36%)	0 / 4 (0.00%)
occurrences (all)	2	4	0
Anaemia			
subjects affected / exposed	2 / 6 (33.33%)	4 / 11 (36.36%)	0 / 4 (0.00%)
occurrences (all)	2	4	0
Leukopenia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	8 / 11 (72.73%)	2 / 4 (50.00%)
occurrences (all)	0	8	2
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	3 / 11 (27.27%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Stomatitis			

subjects affected / exposed	2 / 6 (33.33%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	4 / 11 (36.36%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 6 (83.33%)	8 / 11 (72.73%)	3 / 4 (75.00%)
occurrences (all)	5	8	3
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	2 / 6 (33.33%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 11 (27.27%)	2 / 4 (50.00%)
occurrences (all)	0	3	2
Myalgia			

subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	3 / 11 (27.27%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 6 (33.33%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 11 (18.18%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort D-WT1-D14 Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Bowen's disease			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Flushing			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	4		
Injection site erythema			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

Injection site discomfort subjects affected / exposed occurrences (all) Injection site haematoma subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0		
Investigations Weight decreased subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0		
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all) Sinus tachycardia subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Peripheral sensory neuropathy	 2 / 8 (25.00%) 2		

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Febrile neutropenia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Stomatitis			

subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Myalgia			

subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2011	1. Change in placebo from a lyophilized sucrose formulation reconstituted with a 1/500 dilution of SB62 oil-in-water emulsion to a lyophilized sucrose/mannitol formulation reconstituted with the same dilution of the SB62 oil-in-water emulsion. This change was implemented due to differences in cake height of the lyophilized sucrose formulation compared to lyophilized WT1-A10 and CpG 7909, which would compromise the double blinding of the study. 2. Extension of active follow-up of patients from one to three years. This was requested by the Agence Française de Sécurité Sanitaire des Produits the Santé. 3. In the safety Section (Section 9.1.3), the list of autoimmune diseases to be reported has been replaced by a list of potential immune-mediated diseases (pIMDs). pIMDs include autoimmune diseases and other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology. Moreover, it is specified that all pIMDs will be recorded in the eCRF and reported to GSK Biologicals within 24 hours using the Serious Adverse Event (SAE) screen, regardless of whether the pIMDs are AEs or SAEs. This ensures expedited reporting of all pIMDs. In addition, SAEs related to study treatment are introduced as a separate category of adverse events, to be recorded from receipt of the first study product until the end of follow –up. Contact information for an emergency unblinding request has also been updated. 4. In the sections describing the molecular and immunological read-outs and the translational research, the distinction between the use of fresh tumor samples or Formalin-Fixed, Paraffin Embedded (FFPE) samples for specific tests has been removed. This allows the use of any of these two types of samples in case updated technologies would be employed for specific analyses. Moreover, it is specified that if appropriate, plasma derived from Peripheral Blood Mononuclear Cell (PBMC) purification may be used as backup material for serum in some tests.
26 August 2011	• In case of cardiac assessment during treatment, it has been specified that for patients on 18-week regimens, this assessment should be done between Visit 3 and Visit 4, such that results are available at Visit 4. • Instructions for the processing of tissue samples collected from the resected tumor or tumor bed have been adapted. • Based on feedback from investigators during the investigators' meeting the following additional changes were done: • The extension of a cohort into the Phase II part of the study depends on the outcome of an intermediate assessment of the immunogenicity of the investigational treatment. The serum sample to be used for this evaluation has been changed from a Post-dose 3 sample to a Post-dose 4 sample to ascertain that sufficient time is allowed for an immune response to develop. • The strict timings for screening tests/examinations are made less stringent. All assessments required for screening, except pregnancy testing can be performed within four weeks prior to randomization of the patient. • Exclusion criterion no 13 (Section 4.4) has been rephrased to make clear that only patients receiving therapeutic anticoagulation are excluded from the study. • In the context of postponement of study treatment in an individual patient, the parameters for blood/bone marrow disorders have been adapted for Cohort B and C, such as to avoid frequent postponement of study treatment administration due to side effects of standard treatment. • The tumor imaging at Visit 4 as well as the post-treatment systemic imaging during the presurgery period have been changed from being mandatory to being optional (according to the investigator's discretion). The description of tumor imaging has been clarified.

08 April 2013	• The analysis of the immunogenicity results of the cohort B (unblinded data) evaluating the concurrent administration of the WT1-A10 + AS15 ASCI on day 1 of each cycle of neoadjuvant chemotherapy and during the corticosteroids treatment showed that the above criteria was not fulfilled. Therefore enrolment into the Phase II segment of cohort B has been stopped. But preliminary data has suggested the induction of an anti-WT1 humoral response by the WT1-A10 + AS01B ASCI in absence of concurrent administration of chemotherapy and corticosteroids in two other clinical studies in acute myeloid leukemia. So, the administration of the WT1-A10 + AS15 ASCI will also be evaluated on day 14 of each cycle of neoadjuvant chemotherapy in a new cohort of patients, in order to gain a better understanding of the role of the chemotherapy and corticosteroids on the immune response induced by the WT1-A10 + AS15 ASCI. • The patients in this new cohort, the cohort D, will receive the WT1-A10 + AS15 ASCI at day 14 (D14) of each cycle of the standard neoadjuvant chemotherapy in an open label, non-randomised design. In the absence of a safety signal and if the WT1-A10 + AS15 ASCI induces an adequate immune response according the same rules defined per protocol (see section 3.1.3.1), an additional group of patients with the same eligibility criteria may be recruited in a double blind, randomised phase II segment of the study (Cohort E). These patients will be randomised to receive either WT1-A10 + AS15 ASCI or placebo on D14 of each cycle of neoadjuvant chemotherapy. The patient population eligible for cohorts D and E is presenting a hormone receptor-positive and HER2 non-overexpressing breast cancer. • Also, the assessment of the anti-CpG7909 humoral response and the anti-WT1 T-cell immune response was moved to translational research section as these assessments are not part of the endpoints of the study and will have no direct impact on the study design, i.e. decision making process.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 July 2014	The study was terminated, based on scientific and medical relevance, due to negative Phase III studies which assessed another study product from same technology platform.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The Phase II segment was not completed with only 3 patients enrolled in Cohort A. Consequently, analysis for DFS and OS outcomes was cancelled and the collected clinical activity results are to be considered with caution and uninterpretable.

Notes: