Clinical trial results:
Topotecan plus carboplatin versus standard therapy with paclitaxel plus carboplatin (PC) or gemcitabine plus carboplatin (GC) or pegylated liposomal doxorubicin plus carboplatin (PLDC): a randomized phase III trial of the NOGGO-AGO-Study Group-AGO Austria and GEICO-ENGOT-GCIG intergroup study (HECTOR)

Topotecan plus Carboplatin im Vergleich zur Standardtherapie (Paclitaxel plus Carboplatin oder Gemcitabin plus Carboplatin oder pegyliertes liposomales Doxorubicin plus Carboplatin) in der Therapie von Patientinnen mit Platin-sensitivem rezidivierten epithelialen Ovarialkarzinom, Peritonealkarzinom oder Tubenkarzinom

HECTOR (Hycamtin plus Carboplatin versus Established Regimens for the Treatment of Ovarian Cancer Relapse)

Summary

EudraCT number	2006-004628-34
Trial protocol	DE AT
Global end of trial date	30 June 2015
Results information	
Result version number	v1 (current)
This version publication date	20 May 2023
First version publication date	20 May 2023

Trial information

Trial identification	
Sponsor protocol code	HECTOR_PhaseIII_2006
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00170677
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Prof. Jalid Sehouli, Campus Virchow Klinikum, Augustenburger Platz 1, 13353 Berlin, Charité University Medicine Berlin, Department of Gynecology, European Competence Center for Ovaria, +49 30 450564002, jalid.sehouli@charite.de
Scientific contact	Prof. Jalid Sehouli, Campus Virchow Klinikum, Augustenburger Platz 1, 13353 Berlin, Charité University Medicine Berlin,

Department of Gynecology, European Competence Center for Ovaria, +49 30 450564002, jalid.sehouli@charite.de

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	30 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2015
Global end of trial reached?	Yes
Global end of trial date	30 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Vergleich der progressionsfreien Überlebensrate nach 12 Monaten Nachbeobachtungszeit

Protection of trial subjects:

This study was approved by the local ethics committee and carried out in accordance with local laws and regulations, and the guidelines on Good
Clinical Practice and the Declaration of Helsinki.

Background therapy:

The aim of this multicenter randomized phase III trial was to compare the efficacy and the clinical outcome of topotecan and
carboplatin (TC) compared with established standard platinum based combinations.
The North-Eastern German Society of Gynecological Oncology(NOGGO) has carried out a multicenter phase I/II trial with a
3-day schedule of topotecan in combination with carboplatin which demonstrated the feasibility of this combination and
reported promising response rate of 67%.
- Topotecan (Hycamtin)is an inhibitor of DNA topoisomerase I, an enzyme that allows for relaxation of DNA torsional strain by cleaving and then resealing the DNA molecule. Topotecan is primarily used in the treatment of ovarian cancer and lung cancer.
- Carboplatin or cis-diammine (1,1-cyclobutane dicarboxylate) platinum(II) is administered intravenously.Carboplatin Paraplatin® (AUC 4) is a ‘second generation’ platinum compound, with a different and usually improved toxicity profile.
- Gemcitabine (GEM) is a widely used chemotherapeutic agent for the treatment of various cancers.
- Pegylated liposomal doxorubicin (Caelyx/Doxil). Pegylated liposomes (diameter about 70–100 nm) and liposomal daunorubicin (diameter 45 nm) are small enough to pass intact through defective blood vessels that supply tumors.

Evidence for comparator: -	
Actual start date of recruitment	01 March 2007
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	Spain: 37
Country: Number of subjects enrolled	Austria: 276
Country: Number of subjects enrolled	Germany: 237
Worldwide total number of subjects	550
EEA total number of subjects	550

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)	275
From 65 to 84 years	275
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 62 center in Germany , at 12 center in Spain and at 9 center in Austria.

Pre-assignment

Screening details:

591 female patients with histologically-confirmed ovarian cancer, relapse within 6 month after primary therapy and primary therapy with platin and taxan were screened, from whom 41 patients were excluded . 550 patients were randomly assigned to the experimental and the standard treatment arm in a 1:1 ratio.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TC arm

Arm description:

patients received topotecan 0.75mg/m2/ days 1–3 and carboplatin AUC 5 on day 3 every 3 weeks

Arm type	Experimental
Investigational medicinal product name	TOPOTECAN
Investigational medicinal product code	123948878
Other name	Hycamtin
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

0.75 mg/m2) on days 1 to 3 plus carboplatin equating an area under the curve (AUC) of 5 on day 3 after infusion of topotecan, repeated every 21 days.
Both study drugs were infused over 30 min in 250 ml of 0.9% saline solution.

Investigational medicinal product name	CARBOPLATIN
Investigational medicinal product code	41575944
Other name	Carboplat 50-Lösung; AUC 5
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Topotecan 0.75 mg/m2 /day on days 1–3 and carboplatin AUC 5 on day 3
after topotecan, every 3 weeks. Drugs were infused over 30 min in 250 ml of 0.9% saline solution.

Arm title	standard arm

Arm description:

There were three different treatment possibilities in the standard arm:
- (PC) paclitaxel 175 mg/m2/day on day 1, and carboplatin AUC 5 on day 1, every 3 weeks; (n= 191)
- (GC) gemcitabine 1000 mg/m2/day on day 1 and 8 and carboplatin AUC 4 on day 1, every 3 weeks; (n= 79)
- (PLDC) carboplatin AUC 4 and doxorubicin on day 1, every 3 weeks (n=5)

Arm type	Active comparator

Investigational medicinal product name	CARBOPLATIN
Investigational medicinal product code	41575944
Other name	Carboplat 50/150/450-Lösung; Paraplatin® (AUC 4); AUC 5
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:
carboplatin AUC 4 or AUC 5 on day 1, every 3 weeks.

Investigational medicinal product name	PACLITAXEL
Investigational medicinal product code	33069624
Other name	TAXOL
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:
paclitaxel 175 mg/m2 /day on day 1 and carboplatin AUC 5 on day 1

Investigational medicinal product name	GEMCITABINE
Investigational medicinal product code	95058814
Other name	Gemzar
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:
gemcitabine 1000 mg/m2 /day on day 1 and 8 and carboplatin AUC 4 on day 1, every 3 weeks.

Investigational medicinal product name	Pegyliertes liposomales Doxorubicin
Investigational medicinal product code	25316-40-9
Other name	Doxorubicin Hydrochlorid, CAELYX
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Infusion

Dosage and administration details:
Doxorubicin 2 mg/m2/dayon day 1 carboplatin AUC 4 on day 1, every 3 weeks.

Number of subjects in period 1	TC arm	standard arm
Started	275	275
Completed	275	275

Baseline characteristics

Reporting groups	
Reporting group title	TC arm
Reporting group description:	
patients received topotecan 0.75mg/m2/ days 1–3 and carboplatin AUC 5 on day 3 every 3 weeks	
Reporting group title	standard arm
Reporting group description:	
There were three different treatment possibilities in the standard arm: - (PC) paclitaxel 175 mg/m2/day on day 1, and carboplatin AUC 5 on day 1, every 3 weeks; (n= 191) - (GC) gemcitabine 1000 mg/m2/day on day 1 and 8 and carboplatin AUC 4 on day 1, every 3 weeks; (n= 79) - (PLDC) carboplatin AUC 4 and doxorubicin on day 1, every 3 weeks (n=5)	

Reporting group values	TC arm	standard arm	Total
Number of subjects	275	275	550
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			
median	61	61	
full range (min-max)	29 to 84	24 to 80	-
Gender categorical Units: Subjects			
Female	275	275	550
Male	0	0	0
ECOG performance status Units: Subjects			
status 0	127	154	281
status 1	131	109	240
status 2	15	12	27
not known	2	0	2
FIGO stage at initial diagnosis Units: Subjects			
stage I	21	16	37
stage II	22	17	39
stage III	204	202	406
stage IV	25	39	64
not known	3	1	4

Histology Units: Subjects			
serous-papillary	210	210	420
endometrioid	22	18	40
mucinous	4	5	9
undifferentiated	7	13	20
other (i.e. clear sell, transitional)	32	29	61

End points

End points reporting groups

Reporting group title	TC arm
Reporting group description:	
patients received topotecan 0.75mg/m2/ days 1–3 and carboplatin AUC 5 on day 3 every 3 weeks	
Reporting group title	standard arm
Reporting group description:	
There were three different treatment possibilities in the standard arm: - (PC) paclitaxel 175 mg/m2/day on day 1, and carboplatin AUC 5 on day 1, every 3 weeks; (n= 191) - (GC) gemcitabine 1000 mg/m2/day on day 1 and 8 and carboplatin AUC 4 on day 1, every 3 weeks; (n= 79) - (PLDC) carboplatin AUC 4 and doxorubicin on day 1, every 3 weeks (n=5)	

Primary: progression-free survival (PFS) after 12 months

End point title	progression-free survival (PFS) after 12 months[1]
End point description:	
The PFS rate after 12 months was 37.0% for TC compared with 40.2% in the standard combinations (P = 0.470).	
End point type	Primary
End point timeframe:	
from baseline up to 12 months	
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: more details described in manuscript posted http://www.ncbi.nlm.nih.gov/pubmed/27789470	

End point values	TC arm	standard arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	275		
Units: subjects				
median (confidence interval 95%)	10.0 (9.17 to 10.83)	11 (10.1 to 11.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: overall study , 0–52 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Overall survival (OS), response rate, toxicity, were defined as secondary end points. Severe hematologic toxicities (grade 3/4) were rare in the experimental arm (P < 0.001), with 17.4% leucopenia, 27.8% neutropenia and 15.9% thrombopenia. More information see secondary endpoints

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27789470