



Clinical trial results:

Avelumab as neoadjuvant therapy in subjects with urothelial muscle invasive bladder cancers

Summary

EudraCT number	2017-002758-35
Trial protocol	BE FR
Global end of trial date	05 February 2025

Results information

Result version number	v1 (current)
This version publication date	05 April 2026
First version publication date	05 April 2026
Summary attachment (see zip file)	Avelumab-based neoadjuvant therapy in patients with muscle-invasive bladder cancer (AURA Oncodistinct-004): a phase 2 multicenter clinical trial (article Journal for ImmunoTherapy of Cancer.pdf)

Trial information

Trial identification

Sponsor protocol code	IJB-AURA-ODN-004
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ClinicalTrials.gov: NCT03674424

Notes:

Sponsors

Sponsor organisation name	Institut Jules Bordet
Sponsor organisation address	Rue Meylemeersch 90, Anderlecht, Belgium, 1070
Public contact	CTSU, Institut Jules Bordet, ctsu.trials@hubruxelles.be
Scientific contact	CTSU, Institut Jules Bordet, ctsu.trials@hubruxelles.be

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	19 March 2025
Is this the analysis of the primary completion data?	No
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Global end of trial reached?	Yes
Global end of trial date	05 February 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective: To assess the efficacy of Avelumab (anti-PD-L1) associated to different cytotoxic agents or in monotherapy in patients with non-metastatic MIBC as measured by the pathologic complete response rate (ypT0/Tis ypN0) following neoadjuvant treatment.

Secondary objectives:

- *To determine the pathologic response rate (<ypT2N0) following neoadjuvant treatment in subjects with non-metastatic MIBC.

- *To assess the safety and tolerability of the regimens used

- *To assess the local or distant recurrence or secondary primary malignancy at 12 and 36 months after surgery (or at 12 and 36 months after last treatment dose for subject for whom no surgery was performed)

- *To assess the overall survival with 36 months of follow-up after completion of surgery (or after last treatment dose for subject for whom no surgery was performed).

Protection of trial subjects:

This clinical study was implemented after evaluation by an independent French Committee for the protection of individuals (on 12/06/2018) and an independent Belgian Ethics Committee (on 28/05/2023).

This biomedical research has been authorised by the French competent health authorities, the Agence Nationale de Sécurité des Médicaments et des Produits de Santé (ANSM) on 15/03/2019 and by the Belgian competent health authorities, the Federal Agency for medicines and health products (FAMHP) on 28/05/2023.

Adhering to the principles of ICH-GCP, participants were thoroughly informed before inclusion. This encompassed details such as the voluntary nature of their participation, confidentiality, and protection of personal data, potential risk and benefits of participation, insurance coverage and the possibility of withdrawal at any time. The participants' informed consent was obtained freely, documented in writing, and personally signed and dated by each patient or by an authorized representative under applicable law.

To protect privacy, subject names were not collected; instead, each participant received a unique sequential trial identification number upon registration. This identification number was used for referencing on all case report forms.

Additionally, certain eligibility criteria were established for subjects to participate in the trial, with the aim of minimizing the risk of severe adverse events. The trial protocol included provisions for adjusting treatments in response to specific adverse events. Subjects had the freedom to withdraw from the clinical trial at any time, for any reason, and the study adhered to the principles of the Declaration of Helsinki and the Good Clinical Practice guidelines set forth by the European Union.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 66
Country: Number of subjects enrolled	France: 71
Worldwide total number of subjects	137
EEA total number of subjects	137

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)	48
From 65 to 84 years	89
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

*Actual start date of recruitment to the protocol: 13/07/2018

*Actual date stop date of recruitment to the protocol: 31/08/2021

Pre-assignment

Screening details:

Completion of all necessary screening procedures within 28 days prior to enrolment (unless specifically notified).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

None

Arms

Are arms mutually exclusive?	Yes
Arm title	Cisplatin - eligible : DD-MVAC + A

Arm description:

Cisplatin-eligible subjects: Dose dense methotrexate, vinblastine, doxorubicin, cisplatin (DD-MVAC) + Avelumab

Arm type	Experimental
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

30 mg/m² iv day 1 in combination (DD-MVAC). Each cycle is given every 2 weeks for a maximum of 4 administrations. Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks.

Investigational medicinal product name	Vinblastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

vinblastine 3 mg/m² i.v. day 2 in combination (DD-MVAC). Each cycle is given every 2 weeks for a maximum of 4 administrations. Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

cisplatin 70 mg/m² iv day 2 in combination (DD-MVAC). Each cycle is given every 2 weeks for a maximum of 4 administrations. Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

doxorubicin 30 mg/m² iv day 2 in combination (DD-MVAC). Each cycle is given every 2 weeks for a maximum of 4 administrations. Pegfilgrastim 6 mg subcutaneous (SQ) 24-48 hours after completion of Chemotherapy should be given. Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks.

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	Bavencio 20mg/mL
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab will be administered at a dose of 10 milligram per kilogram (10 mg/kg) 1-hour intravenous (i.v.) infusion once every 2 weeks. Dose reductions are not allowed. In combination with Chemotherapy, Avelumab will be given before the Chemotherapy.

Arm title	Cisplatin - eligible: CG + A
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Arm description:

Cisplatin-eligible subjects: Cisplatin, Gemcitabine (CG) + Avelumab

Arm type	Experimental
Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	Bavencio 20mg/mL
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab will be administered at a dose of 10 milligram per kilogram (10 mg/kg) 1-hour intravenous (i.v.) infusion once every 2 weeks. Dose reductions are not allowed. In combination with Chemotherapy, Avelumab will be given before the Chemotherapy.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000 mg/m² iv in day 1 and day 8 in combination (CG). Each cycle is given every 3 weeks for a maximum of 4 administrations. Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 70 mg/m² iv in day 1 in combination (CG). Each cycle is given every 3 weeks for a maximum of 4 administrations. Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks.

Arm title	Cisplatin - ineligible: PG + A
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Arm description:

Cisplatin-ineligible subjects: Paclitaxel, Gemcitabine (PG) + Avelumab

Arm type	Experimental
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Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	Bavencio 20mg/mL
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab will be administered at a dose of 10 milligram per kilogram (10 mg/kg) 1-hour intravenous (i.v.) infusion once every 2 weeks. Dose reductions are not allowed. In combination with Chemotherapy, Avelumab will be given before the Chemotherapy.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine 1000 mg/m² iv in day 1 and day 15 in combination (PG). Each cycle is given every 4 weeks for a maximum of 4 administrations (2 cycles). Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks for 4 administrations.

Investigational medicinal product name	paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 80 mg/m² iv in day 1 and day 15 in combination (PG). Each cycle is repeated every 4 weeks for a maximum of 4 administrations (2 cycles). Chemotherapy is associated with Avelumab 10 mg/kg i.v. given every 2 weeks for 4 administrations.

Arm title	Cisplatin - ineligible: A
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Arm description:

Cisplatin-ineligible subjects: Avelumab

Arm type	Experimental
Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	Bavencio 20mg/mL
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avelumab will be administered at a dose of 10 milligram per kilogram (10 mg/kg) 1-hour intravenous (i.v.) infusion once every 2 weeks. Dose reductions are not allowed. Avelumab is not associated with any chemotherapy within this arm.

Number of subjects in period 1	Cisplatin - eligible : DD-MVAC + A	Cisplatin - eligible: CG + A	Cisplatin - ineligible: PG + A
Started	39	40	29
Completed	38	36	28
Not completed	1	4	1
Consent withdrawn by subject	1	2	1
Physician decision	-	1	-
Technical problems	-	1	-

Not resectable at entry study (no treatment)	-	-	-
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Number of subjects in period 1	Cisplatin - ineligible: A
Started	29
Completed	28
Not completed	1
Consent withdrawn by subject	-
Physician decision	-
Technical problems	-
Not resectable at entry study (no treatment)	1

Baseline characteristics

Reporting groups

Reporting group title	Cisplatin - eligible : DD-MVAC + A
Reporting group description:	
Cisplatin-eligible subjects: Dose dense methotrexate, vinblastine, doxorubicin, cisplatin (DD-MVAC) + Avelumab	
Reporting group title	Cisplatin - eligible: CG + A
Reporting group description:	
Cisplatin-eligible subjects: Cisplatin, Gemcitabine (CG) + Avelumab	
Reporting group title	Cisplatin - ineligible: PG + A
Reporting group description:	
Cisplatin-ineligible subjects: Paclitaxel, Gemcitabine (PG) + Avelumab	
Reporting group title	Cisplatin - ineligible: A
Reporting group description:	
Cisplatin-ineligible subjects: Avelumab	

Reporting group values	Cisplatin - eligible : DD-MVAC + A	Cisplatin - eligible: CG + A	Cisplatin - ineligible: PG + A
Number of subjects	39	40	29
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	24	17	3
From 65-84 years	15	23	26
85 years and over	0	0	0
Age continuous			
Units: years			
median	63	68	72
full range (min-max)	47 to 77	41 to 81	41 to 80
Gender categorical			
Units: Subjects			
Female	9	11	2
Male	30	29	27
ECOG PS			
Units: Subjects			
Zero	36	32	15
One	3	8	14
Clinical Tumour stage			
Units: Subjects			
T2 N0 M0	20	20	12
T2 N0 M: missing	1	0	0
T2 NX M0	11	8	6

T2 NX M:missing	0	2	0
T3/T4 N0 M0	1	2	4
T3/T4 NX M0	0	2	2
T2 N1 M0	3	1	2
T3/T4 N1 M0	2	0	0
T2 N2/3 M0	1	4	3
T3/T4 N2 M0	0	1	0
Histological type			
Units: Subjects			
Muscle-invasive urothelial carcinoma	32	38	23
Urothelial carcinoma with mixed histology	7	2	6
BMI at screening			
Units: cm/kg ²			
median	26.7	26.5	25.9
full range (min-max)	19.2 to 50.2	18 to 36.8	17.9 to 36.5
At screening: GFR			
Units: ml/min			
median	85	89	67
full range (min-max)	60 to 166	60 to 154	34 to 94

Reporting group values	Cisplatin - ineligible: A	Total	
Number of subjects	29	137	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	48	
From 65-84 years	25	89	
85 years and over	0	0	
Age continuous			
Units: years			
median	74		
full range (min-max)	49 to 80	-	
Gender categorical			
Units: Subjects			
Female	3	25	
Male	26	112	
ECOG PS			
Units: Subjects			
Zero	11	94	
One	18	43	
Clinical Tumour stage			
Units: Subjects			
T2 N0 M0	12	64	

T2 N0 M: missing	0	1	
T2 NX M0	12	37	
T2 NX M:missing	0	2	
T3/T4 N0 M0	2	9	
T3/T4 NX M0	1	5	
T2 N1 M0	0	6	
T3/T4 N1 M0	2	4	
T2 N2/3 M0	0	8	
T3/T4 N2 M0	0	1	
Histological type			
Units: Subjects			
Muscle-invasive urothelial carcinoma	25	118	
Urothelial carcinoma with mixed histology	4	19	
BMI at screening			
Units: cm/kg ²			
median	27.7		
full range (min-max)	22.3 to 34	-	
At screening: GFR			
Units: ml/min			
median	64		
full range (min-max)	29 to 115	-	

End points

End points reporting groups

Reporting group title	Cisplatin - eligible : DD-MVAC + A
Reporting group description: Cisplatin-eligible subjects: Dose dense methotrexate, vinblastine, doxorubicin, cisplatin (DD-MVAC) + Avelumab	
Reporting group title	Cisplatin - eligible: CG + A
Reporting group description: Cisplatin-eligible subjects: Cisplatin, Gemcitabine (CG) + Avelumab	
Reporting group title	Cisplatin - ineligible: PG + A
Reporting group description: Cisplatin-ineligible subjects: Paclitaxel, Gemcitabine (PG) + Avelumab	
Reporting group title	Cisplatin - ineligible: A
Reporting group description: Cisplatin-ineligible subjects: Avelumab	

Primary: pathological complete response

End point title	pathological complete response
End point description: pathological complete response: ypT0/TisN0. The primary endpoint was pCR, defined as the absence of invasive residual disease (ypT0/Tis) and no microscopic lymph node involvement (ypN0) in the surgical specimen of evaluable patients. Patients who received at least one dose of each medication in their respective treatment arm and underwent cystectomy were considered evaluable. Patients experiencing early progression that precluded surgery were considered evaluable and assessed as therapeutic failures.	
End point type	Primary
End point timeframe: at surgery	

End point values	Cisplatin - eligible : DD-MVAC + A	Cisplatin - eligible: CG + A	Cisplatin - ineligible: PG + A	Cisplatin - ineligible: A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38 ^[1]	36 ^[2]	28 ^[3]	28 ^[4]
Units: patients	38	36	28	28

Notes:

[1] - evaluable patients

[2] - evaluable patients

[3] - evaluable patients

[4] - evaluable patients

Statistical analyses

Statistical analysis title	pCR - Cisplatin eligible - ddMVAC-A
Statistical analysis description: In Cisplatin eligible cohort ddmvac Pathological response rates were estimated with 95%CIs using Wilson method. The null hypothesis should be rejected if the true pCR rate was $\geq 45\%$. A two-stage Simon design was applied for each	

treatment regimen.

Comparison groups	Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A v Cisplatin - eligible : DD-MVAC + A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[5]
Parameter estimate	pathological complete response rate
Point estimate	58
Confidence interval	
level	95 %
sides	2-sided
lower limit	42
upper limit	72

Notes:

[5] - Single-arm phase II trial with hypothesis testing against a historical threshold

Statistical analysis title	pCR - Cisplatin eligible- GC-A
Statistical analysis description: Pathological response rates were estimated with 95%CIs using Wilson method. The null hypothesis should be rejected if the true pCR rate was $\geq 45\%$. A two-stage Simon design was applied for each treatment regimen. N = 36	
Comparison groups	Cisplatin - eligible: CG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[6]
Parameter estimate	pCR
Point estimate	53
Confidence interval	
level	95 %
sides	2-sided
lower limit	37
upper limit	68

Notes:

[6] - Single-arm phase II trial with hypothesis testing against a historical threshold

Statistical analysis title	pCR Cisplatin-ineligible cohort - PG-A
Statistical analysis description: Pathological response rates were estimated with 95%CIs using Wilson method. The null hypothesis should be rejected if the true pCR rate was $\geq 45\%$. A two-stage Simon design was applied for each treatment regimen. N = 28	
Comparison groups	Cisplatin - ineligible: PG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[7]
Parameter estimate	pathological complete response rate
Point estimate	14

Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	31

Notes:

[7] - Single-arm phase II trial with hypothesis testing against a historical threshold

Statistical analysis title	pCR - Cisplatin-ineligible cohort- A
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Statistical analysis description:

Pathological response rates were estimated with 95%CIs using Wilson method. The null hypothesis should be rejected if the true pCR rate was $\geq 45\%$. A two-stage Simon design was applied for each treatment regimen.

N=28

Comparison groups	Cisplatin - ineligible: A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[8]
Parameter estimate	pathological complete response rate
Point estimate	32
Confidence interval	
level	95 %
sides	2-sided
lower limit	18
upper limit	51

Notes:

[8] - Single-arm phase II trial with hypothesis testing against a historical threshold

Statistical analysis title	Time-to-event : EFS 12 months GC-A
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Statistical analysis description:

the Kaplan- Meier method, with censoring for patients without predefined events or lost to follow- up at the data cut- off.

12 months EFS with 95%CI.

N = 36

Comparison groups	Cisplatin - eligible: CG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	EFS (%)
Point estimate	84
Confidence interval	
level	95 %
sides	2-sided
lower limit	73
upper limit	97

Statistical analysis title	Time-to-event : EFS at 36 months GC-A
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Statistical analysis description:

Time to event analyses using kaplan meier estimate and the EFS at 36 months with a 95% CI.

N = 36

Comparison groups	Cisplatin - eligible: CG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[9]
Parameter estimate	EFS (%)
Point estimate	65
Confidence interval	
level	95 %
sides	2-sided
lower limit	51
upper limit	82

Notes:

[9] - Descriptive survival analyses

Statistical analysis title	Time-to-event : EFS 12 months ddMVAC-A
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Statistical analysis description:

Kaplan-Meier method, EFS at 12 months with 95CI.

N = 38

Comparison groups	Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[10]
Parameter estimate	EFS (%)
Point estimate	92
Confidence interval	
level	95 %
sides	2-sided
lower limit	84
upper limit	100

Notes:

[10] - Descriptive survival analyses

Statistical analysis title	Time-to-event : EFS 36 months ddMVAC-A
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Statistical analysis description:

Kaplan-Meier Method

N = 28

Comparison groups	Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[11]
Parameter estimate	EFS (%)
Point estimate	81

Confidence interval	
level	95 %
sides	2-sided
lower limit	69
upper limit	95

Notes:

[11] - Descriptive survival analyses

Statistical analysis title	Time-to-event : EFS at 12 months PG-A
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Statistical analysis description:

Kaplan meier method.

N = 28

Comparison groups	Cisplatin - ineligible: PG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[12]
Parameter estimate	EFS (%)
Point estimate	60
Confidence interval	
level	95 %
sides	2-sided
lower limit	44
upper limit	81

Notes:

[12] - Descriptive survival analyses

Statistical analysis title	Time-to-event : EFS 36 months PG-A
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Statistical analysis description:

Kaplan-meier estimation and presentation with Event Free Survival at 12 month and 36 month with 95%CI.

N = 28

Comparison groups	Cisplatin - ineligible: PG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[13]
Parameter estimate	EFS (%)
Point estimate	41
Confidence interval	
level	95 %
sides	2-sided
lower limit	26
upper limit	65

Notes:

[13] - Descriptive survival analyses

Statistical analysis title	Time-to-event : EFS 12 months A
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Statistical analysis description:

Kaplan-meier estimation and presentation with Event Free Survival at 12 month and 36 month with 95%CI

N = 28

Comparison groups	Cisplatin - ineligible: A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[14]
Parameter estimate	EFS (%)
Point estimate	64
Confidence interval	
level	95 %
sides	2-sided
lower limit	49
upper limit	85

Notes:

[14] - Descriptive survival analyses

Statistical analysis title	Time-to-event : EFS 36 months A
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Statistical analysis description:

Kaplan-meier estimation and presentation with Event Free Survival at 12 month and 36 month with 95%CI
N = 28

Comparison groups	Cisplatin - ineligible: A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[15]
Parameter estimate	EFS (%)
Point estimate	43
Confidence interval	
level	95 %
sides	2-sided
lower limit	28
upper limit	66

Notes:

[15] - Descriptive survival analyses

Statistical analysis title	Time-to-event : OS 12 months ddMVAC-A
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Statistical analysis description:

Kaplan-meier estimation and presentation with overall survival at 12 month and 36 month with 95%CI
N = 38

Comparison groups	Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[16]
Parameter estimate	OS(%)
Point estimate	95
Confidence interval	
level	95 %
sides	2-sided
lower limit	88
upper limit	100

Notes:

[16] - descriptive

Statistical analysis title	Time-to-event : OS 36 months ddMVAC-A
Statistical analysis description: Kaplan-meier estimation and presentation with overall Survival at 12 month and 36 month with 95%CI N= 38	
Comparison groups	Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[17]
Parameter estimate	OS(%)
Point estimate	87
Confidence interval	
level	95 %
sides	2-sided
lower limit	76
upper limit	98

Notes:

[17] - Descriptive

Statistical analysis title	Time-to-event : OS 12 months GC-A
Statistical analysis description: Kaplan-meier estimation and presentation with Overall Survival at 12 month and 36 month with 95%CI N = 36	
Comparison groups	Cisplatin - eligible: CG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[18]
Parameter estimate	OS(%)
Point estimate	92
Confidence interval	
level	95 %
sides	2-sided
lower limit	84
upper limit	100

Notes:

[18] - Descriptive

Statistical analysis title	Time-to-event : OS 36 months GC-A
Statistical analysis description: Kaplan-meier estimation and presentation with overall Survival at 12 month and 36 month with 95%CI N = 36	
Comparison groups	Cisplatin - eligible: CG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - ineligible: PG + A v Cisplatin - ineligible: A

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[19]
Parameter estimate	OS(%)
Point estimate	67
Confidence interval	
level	95 %
sides	2-sided
lower limit	53
upper limit	84

Notes:

[19] - Descriptive

Statistical analysis title	Time-to-event : OS 12 months PG-A
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Statistical analysis description:

Kaplan-meier estimation and presentation with overall Survival at 12 month and 36 month with 95%CI
N=28

Comparison groups	Cisplatin - ineligible: PG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[20]
Parameter estimate	OS(%)
Point estimate	82
Confidence interval	
level	95 %
sides	2-sided
lower limit	68
upper limit	98

Notes:

[20] - Descriptive

Statistical analysis title	Time-to-event : OS 36 months PG-A
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Statistical analysis description:

Kaplan-meier estimation and presentation with overall Survival at 12 month and 36 month with 95%CI
N = 28

Comparison groups	Cisplatin - ineligible: PG + A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[21]
Parameter estimate	OS(%)
Point estimate	48
Confidence interval	
level	95 %
sides	2-sided
lower limit	33
upper limit	71

Notes:

[21] - Descriptive

Statistical analysis title	Time-to-event : OS 12 months A
Statistical analysis description: Kaplan-meier estimation and presentation with overall Survival at 12 month and 36 month with 95%CI N = 28	
Comparison groups	Cisplatin - ineligible: A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[22]
Parameter estimate	OS(%)
Point estimate	78
Confidence interval	
level	95 %
sides	2-sided
lower limit	65
upper limit	95
Notes:	
[22] - Descriptive survival analyses	

Statistical analysis title	Time-to-event : OS 36 months A
Statistical analysis description: Kaplan-meier estimation and presentation with overall Survival at 12 month and 36 month with 95%CI. N = 28	
Comparison groups	Cisplatin - ineligible: A v Cisplatin - eligible : DD-MVAC + A v Cisplatin - eligible: CG + A v Cisplatin - ineligible: PG + A
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other ^[23]
Parameter estimate	OS(%)
Point estimate	42
Confidence interval	
level	95 %
sides	2-sided
lower limit	27
upper limit	65
Notes:	
[23] - Descriptive survival analyses	

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall study

Adverse event reporting additional description:

The adverse events are not reported in format that fits this platform. Please see attached documents for full analysis.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28
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Reporting groups

Reporting group title	Cisplatin-eligible cohort ddMVAC A
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Reporting group description:

Cisplatin-eligible cohort ddMVAC A N = 39

Reporting group title	Cisplatin-eligible cohort GC-A
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Reporting group description:

Cisplatin-eligible cohort GC-A

Reporting group title	Cisplatin-ineligible cohort PG-A
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Reporting group description: -

Reporting group title	Cisplatin-ineligible cohort A
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Reporting group description:

Cisplatin-ineligible cohort A

Serious adverse events	Cisplatin-eligible cohort ddMVAC A	Cisplatin-eligible cohort GC-A	Cisplatin-ineligible cohort PG-A
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 39 (46.15%)	19 / 40 (47.50%)	10 / 28 (35.71%)
number of deaths (all causes)	6	13	16
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Acute kidney injury			
subjects affected / exposed	6 / 39 (15.38%)	6 / 40 (15.00%)	6 / 28 (21.43%)
occurrences causally related to treatment / all	2 / 6	3 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 39 (5.13%)	2 / 40 (5.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	3 / 39 (7.69%)	0 / 40 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Sepsis			
subjects affected / exposed	2 / 39 (5.13%)	2 / 40 (5.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 39 (2.56%)	2 / 40 (5.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	5 / 39 (12.82%)	3 / 40 (7.50%)	5 / 28 (17.86%)
occurrences causally related to treatment / all	5 / 5	1 / 3	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cisplatin-ineligible cohort A		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 28 (21.43%)		
number of deaths (all causes)	16		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Acute kidney injury			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Sepsis			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Cisplatin-eligible cohort ddMVAC A	Cisplatin-eligible cohort GC-A	Cisplatin-ineligible cohort PG-A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 39 (100.00%)	40 / 40 (100.00%)	27 / 28 (96.43%)
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	11 / 39 (28.21%)	24 / 40 (60.00%)	1 / 28 (3.57%)
occurrences (all)	11	24	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	18 / 39 (46.15%)	21 / 40 (52.50%)	5 / 28 (17.86%)
occurrences (all)	18	21	5
Constipation			
subjects affected / exposed	18 / 39 (46.15%)	15 / 40 (37.50%)	6 / 28 (21.43%)
occurrences (all)	18	15	6

Psychiatric disorders			
Asthenia			
subjects affected / exposed	32 / 39 (82.05%)	32 / 40 (80.00%)	20 / 28 (71.43%)
occurrences (all)	32	32	20
Anorexia			
subjects affected / exposed	14 / 39 (35.90%)	19 / 40 (47.50%)	6 / 28 (21.43%)
occurrences (all)	14	19	6

Non-serious adverse events	Cisplatin-ineligible cohort A		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 28 (89.29%)		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Psychiatric disorders			
Asthenia			
subjects affected / exposed	15 / 28 (53.57%)		
occurrences (all)	15		
Anorexia			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2018	Belgium : Halt accrual in the cisplatin ineligible cohort (following FR competent authority disapproval of the study)
25 January 2019	Belgium: *Request to restart accrual in the cisplatin ineligible cohort *New/Amended patient information sheet/informed consent (including addendum) *New/Amended study documents *New/Amended information related to IMP or IMPD *New/Amended IDMC charter
12 March 2019	Belgium: *New/Amended patient information sheet/informed consent (including addendum) *New/Amended study documents *New/Amended protocol *Addition of participating centre
03 June 2019	France: New/Amended Reference Safety Information
26 September 2019	Belgium: *New/Amended patient information sheet/informed consent (including addendum) *Addition of participating centre
13 November 2019	France: *Closure of an approved site *New/Amended Reference Safety Information *New/Amended patient information sheet/informed consent (including addendum) *New/Amended protocol *Change of Principal Investigator
19 November 2019	Belgium: *New/Amended patient information sheet/informed consent (including addendum) *New/Amended study documents *New/Amended protocol *New/Amended Reference Safety Information
16 June 2020	France: *New/Amended patient information sheet/informed consent (including addendum) *New/Amended protocol *New/Amended other study documents *New/Amended Reference Safety Information
28 July 2020	Belgium: *New/Amended patient information sheet/informed consent (including addendum) *New/Amended protocol *New/Amended Reference Safety Information
30 March 2021	France: New/Amended Reference Safety Information
06 April 2021	Belgium: New/Amended Reference Safety Information
29 November 2021	Belgium: Addition of participating centre

17 March 2023	Belgium: *Change of national coordinator *Change in trial logistic (not site related) *New/Amended protocol
24 March 2023	France: *New/Amended protocol *New/Amended patient information sheet/informed consent (including addendum)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

There were no limitations and caveats.

Notes: