BARCELONA 2024 ESMO congress
BARCELONA SPAIN
13-17 SEPTEMBER 2024

Centre Baclesse unicancer NORMANDIE - CAEN

Poster FPN #1977P
ClinicalTrials.gov NCT04678362

Efficacy of talazoparib and avelumab as a maintenance treatment in patients with advanced/metastatic urothelial carcinoma (mUC) whose disease did not progress after a first-line platinum-based chemotherapy (PBCT): The GETUG-TALASUR trial.

Elodie COQUAN (MD)[1], Elouen BOUGHALEM (MD)[2], Damien POUESSEL (MD, PhD)[3], Justine LEQUESNE (PhD)[4], Fabien CALCAGNO (MD, PharmD)[5], Jean-Michel GRELLARD (MSc)[4], François CHRISTY (MSc)[4], Hakim MAHAMMEDI (MD)[6], Sylvain LADOIRE (MD, PhD)[7], Delphine BORCHIELLINI (MD)[8], Raphaël LEMAN (PharmD, PhD)[9],Céline BAZILLE (MD, PhD)[10], Jacqueline FONTUGNE (MD, PhD)[11] , Laurence CROUZET (MD)[12], Aude FLECHON (MD, PhD)[13], Camille SERRATE (MD)[14], Gwenaelle GRAVIS (MD)[15], Bénédicte CLARISSE (PharmD, PhD)[4], Antoine THIERRY VUILLEMIN[5], Florence JOLY (MD, PhD)[1]

[1]Medical Oncology Department, Centre François Baclesse, F-14000, Caen, France, [2]Medical Oncology Department, Institut de Cancérologie de l'Ouest, F-44000, Nantes, France, [3]Medical Oncology Department, Institut Universitaire de Cancérologie de Toulouse - Oncopole (IUCT- Oncopole), Oncopole Claudius Regaud, F-31000, Toulouse, France, [4]Clinical Research Department Centre François Baclesse, University Unicaen, F-14000, Caen, France, [5]Medical Oncology Department, University Hospital Jean Minjoz, F-25000, Besançon, France, [6]Medical Oncology Department, Centre Jean Perrin, F-63000, Clermont-Ferrand, France, [7]Medical Oncology Department, Centre Georges-François Leclerc, F-21000, Dijon, France , [8]Medical Oncology Department, Centre Antoine Lacassagne, F-06000, Nice, France, [9]Genetic and oncology biology Department, Centre François Baclesse, F-14000, Caen, France, [10]Department of Pathology, CHU de Caen, F-14000, Caen, France, [11]Pathology Department, Institut Curie Saint-Cloud, UMR144 , Molecular Oncology Team, F-92210, Saint-Cloud, France, [12]Medical Oncology Department, Centre Eugène Marquis, F-35000, Rennes, France, [13]Medical Oncology Department, Centre Léon Bérard, F-69000, Lyon, France, [14]Medical Oncology Department, Hôpital des Diaconesses, Croix Saint-Simon, F-75020, Paris, France, [15]Medical Oncology Department, Institut Paoli Calmettes, F-13000, Marseille, France

BACKGROUND

Avelumab, an anti-PDL1 antibody, is the standard maintenance treatment after a 1st line platinum-based chemotherapy (PBCT) in patients with advanced/metastatic urothelial carcinoma (mUC). **Talazoparib** is an oral PARP inhibitor already approved in BRCA mutated breast cancer. Based on preclinical and clinical data of the synergy between PARP and immune checkpoint inhibitors, this single-arm phase II trial aimed to assess the efficacy of Talazoparib plus Avelumab combination as a maintenance treatment in patients with mUC who obtained objective response (OR) or stable disease (SD) after a 1st -line PBCT.

OBJECTIVES

Main objective

- Efficacy, defined as progression-free survival (PFS) of a maintenance treatment combining Talazoparib and Avelumab in patients with locally advanced/metastatic urothelial carcinoma with a stable or objective response to a platinum-based chemotherapy.

Secondary objectives

- Safety profile of the combination
- Overall survival (OS)
- Objective response rate (ORR)

Ancillary tumor analysis

- Exploration of HRD status and gene mutations

STUDY DESIGN

Multicenter, single arm phase II trial[1]

Study population

- Platinum-sensitive metastatic or locally advanced urothelial carcinoma
- Stage IV disease
- Having received platinum-based chemotherapy
- Stable disease (SD) or partial response (PR) or complete response (CR) to chemotherapy
- All comers patients

Treatment schedule

Patients enrolled within 8 weeks after the last dose of chemotherapy
Combined treatment start within 28 days after inclusion.

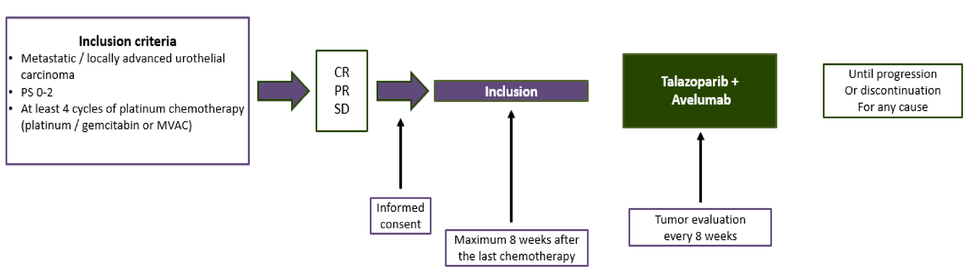
➢ **Talazoparib dosage**

1 mg orally once daily in a 28-day cycle.
In case of mild renal impairment (CLcr ≤ 30-59 mL/min) at inclusion, patients received the daily dose of 0.75 mg.
Dose adjustments for toxicities:

- 1st dose reduction: 0,75 mg/day
- 2nd dose reduction: 0,5 mg/day
- 3rd dose reduction: 0,25 mg/day

➢ **Avelumab dosage**

800 mg per IV route, on D1 and D15, in a 28-day cycle.
No dose adaptation



Statistical considerations

Sample size

We used a one arm survival design, considering a median PFS from start of combined treatment of

- 4 months as unacceptable (H_0 hypothesis)
- 7 months as expected (H_1 hypothesis)
- Alpha level of 5% and power of 80%.

→ 45 assessable patients required.

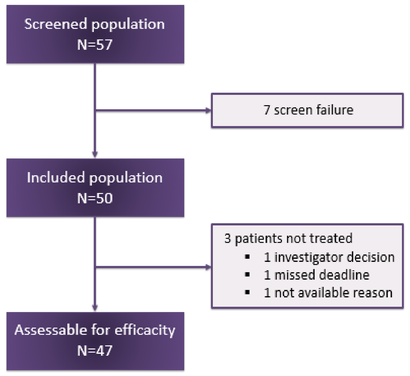
→ To anticipate 10% of non-assessable patients, we planned to enroll 50 patients overall over 18 months of inclusion.

Decision criteria

→ The median PFS should be longer than 5.9 months to conclude to efficacity.

FLOW-CHART

50 patients enrolled in 13 French centres from June 2021 to July 2023



POPULATION

Patients characteristics at inclusion	n = 47
Age (y) - median (min-max)	69 (40-82)
Sex - n (%)	
Male	37 (78.7%)
Female	10 (21.3%)
Performans status - n (%)	
0	14 (29.8%)
1	33 (70.2%)
1st-line chemotherapy - n (%)	
Carboplatin	25 (53%)
Cisplatin	22 (47%)
Best tumoral response - n (%)	
Complete response	5 (10.9%)
Partial response	15 (32.6%)
Stable disease	24 (52.2%)
Not assessable	2 (4.3%)

EFFICACY

After a median follow-up of 17.3 months (95% CI : 2-36),

→ Disease progression (PD): 33 patients (70%)

→ Death: 24 patients (51.1%)

→ Median overall survival : 29.9 months

Objective response rate (ORR)

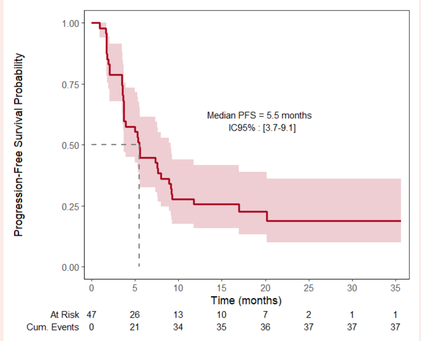
Response	n=47*
CR	10 (22.2%)
PR	1 (2.2%)
SD	23 (51.1%)
PD	11 (24.4%)

*2 not assessable for response evaluation

ORR 24.4%

Median duration of response : 9.6 months

Progression-Free Survival



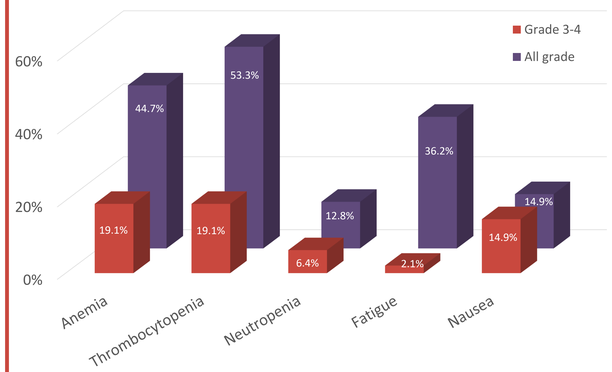
TREATMENT ADJUSTMENT

n=47	Talazoparib	Avelumab
Dose reduction – n (%)	25 (53.2%)	0 (0%)
Definitive interruption n (%)	3[a] (6.3%)	2[b] (4.3%)

[a] Grade 4 thrombocytopenia, grade 3 asthenia, grade 3 renal failure
[b] Grade 3 interstitial lung disease, grade 2 nausea

SAFETY

Most common Talazoparib and/or Avelumab related AEs



→ Immune-related AEs Gr2-3 were reported in 6 pts

Immune-related AEs	Grade
Interstitial lung disease	2
Nausea	2
Infusion related reaction	2
Hyperglycemia	2
Hyperlipasemia	2 & 3

CONCLUSIONS

Talazoparib plus Avelumab in maintenance treatment of advanced/metastatic urothelial carcinoma did not reach the 5.9 months expected PFS threshold. Results are consistent with the clinical outcomes of Avelumab monotherapy reported in the JAVELIN bladder100 trial[2] and are not in favor of adding PARPi to Avelumab in this mUC population.

ANCILLARY TUMOR ANALYSIS

17 available tumor samples :

→ 2 tumor samples (12%) BRCA mutated
→ 5 tumor samples (29%) with high HRD (nLST≥15)

No link was observed with clinical outcomes.

Funding - Acknowledgments

This trial (NCT04678362) is granted by Pfizer SAS that also provides Talazoparib and Avelumab for participating patients.

We acknowledge the GETUG (Groupe d'Etude des Tumeurs Uro-Génitales) for its support in scientific collaboration. We thank the Data Processing Centre (DPC) of the North West Canceropole (Centre de Traitement des Données du Cancéropôle Nord-Ouest) in charge of data management. We also thank the members of the Independent Data Monitoring Committee. We are grateful to all the patients who consented to participate.

References

[1] Coquan E, Clarisse B, Lequesne J, Brachet PE, Nevière Z, Meriaux E, Bonnet I, Castera M, Goardon N, Boutrois J, Travers R, Joly F, Grellard JM, Thiery-Vuillemin A. TALASUR trial: a single arm phase II trial assessing efficacy and safety of TALazoparib and Avelumab as maintenance therapy in platinum-Sensitive metastatic or locally advanced URothelial carcinoma. BMC Cancer. 2022 Nov 24;22(1):1213. doi: 10.1186/s12885-022-10216-z. PMID: 36434554; PMCID: PMC9700963.

[2] Powles T, Park SH, Caserta C, Valderrama BP, Gurney H, Ullén A, Loriot Y, Sridhar SS, Sternberg CN, Bellmunt J, Aragon-Ching JB, Wang J, Huang B, Laliberte RJ, di Pietro A, Grivas P. Avelumab First-Line Maintenance for Advanced Urothelial Carcinoma: Results From the JAVELIN Bladder 100 Trial After ≥2 Years of Follow-Up. J Clin Oncol. 2023 Jul 1;41(19):3486-3492. doi: 10.1200/JCO.22.01792. Epub 2023 Apr 18. PMID: 37071838; PMCID: PMC10306435.

Contact information

Dr Elodie COQUAN
e.coquan@baclesse.unicancer.fr