READY: REAl-world Data from an Italian compassionate use program of avelumab first-line maintenance treatment for locallY advanced or metastatic urothelial carcinoma (la/mUC)

L. Antonuzzo,[1] M. Maruzzo,[2] U. De Giorgi,[3] D. Santini,[4] R. Tambaro,[5] S. Buti,[6] F. Carrozza,[7] F. Calabrò,[8] G. Di Lorenzo,[9] G. Fornarini,[10] R. Iacovelli,[11] D. Cullurà,[12] C. Messina,[13] C. Masi,[14] A. Ciccia,[14] G. Fazzi,[15] F. Venturini,[15] R. Colasanto,[15] A. Necchi,[16] S. Bracarda[17]

[1]Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; [2]Istituto Oncologico Veneto, Padova, Italy; [3]IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" – IRST, Meldola, Italy; [4]Università La Sapienza-Polo Pontino, Rome, Italy; [5]Istituto Nazionale Tumori Fondazione G. Pascale, Naples, Italy; [6]University of Parma, Parma, Italy; [7]AUSL della Romagna, Ravenna, Italy; [8]Azienda Ospedaliera San Camillo Forlanini, Rome, Italy; [9]ASL SALERNO - P.O. "A. Tortora," Pagani, Italy; [10]Ospedale Policlinico San Martino, Genoa, Italy; [11]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [12]Istituto Europeo di Oncologia (IEO), Milan, Italy; [13]Ospedale A.R.N.A.S. Civico, Palermo, Italy; [14]Pfizer Italia srl, Rome, Italy; [15]Merck Serono S.p.A., Rome, Italy, an affiliate of Merck KGaA, Darmstadt, Germany; [16]IRCCS San Raffaele Hospital and Scientific Institute, Milan, Italy; [17]Azienda Ospedaliera Santa Maria, Terni, Italy

SCOPE

- **This study reports baseline characteristics and outcomes in patients with la/mUC who received avelumab first-line (1L) maintenance in an Italian compassionate use program (CUP), before reimbursement from the Italian Medicines Agency was available**

CONCLUSIONS

- **This CUP included a large patient population with la/mUC from 140 Italian oncology centers representative of daily clinical practice, and results are consistent with those of previous studies[1,2]**
- **Avelumab 1L maintenance provided clinical benefits and had a manageable safety profile in Italian patients with la/mUC, consistent with findings from the phase 3 JAVELIN Bladder 100 trial[1,2]**
  - **Median overall survival (OS) was not reached, with a 12-month OS rate of 69.2% (95% CI, 64.8%-73.7%)**
  - **Median progression-free survival (PFS) was 8.1 months (95% CI, 6.1-10.4 months)**
- **Clinical benefits were observed in a population that included high proportions of patients who had upper tract UC or received carboplatin-based chemotherapy**
- **Overall, these real-world data provide further support for avelumab 1L maintenance as standard of care in eligible patients with la/mUC**

Correspondence:
Ugo De Giorgi, **ugo.degiorgi@irst.emr.it**

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BACKGROUND

- Bladder cancer is the fifth most common cancer in Italy, with 28,336 new cases and 7,108 deaths estimated in 2020; UC is the most common type of bladder cancer (>90%)[3-5]
- In the phase 3 JAVELIN Bladder 100 trial, avelumab 1L maintenance + best supportive care (BSC) significantly prolonged OS and PFS vs BSC alone in patients with la/mUC that had not progressed with 1L platinum-based chemotherapy[1,2]
  - After long-term follow-up (median follow-up, ≥38 months in both arms), median OS was 23.8 months with avelumab + BSC vs 15.0 months with BSC alone (hazard ratio [HR], 0.76 [95% CI, 0.631-0.915]; p=0.0036), and median PFS was 5.5 months vs 2.1 months (HR, 0.54 [95% CI, 0.457-0.645]; p<0.0001), respectively (both measured from start of maintenance treatment)[2]
  - Based on the results from the JAVELIN Bladder 100 trial, avelumab 1L maintenance was approved for patients with la/mUC in various countries worldwide, and it is now recommended as standard of care in international treatment guidelines[6-10]
- Here, we report real-world patient characteristics and outcomes in patients with la/mUC who received avelumab 1L maintenance in an Italian CUP before reimbursement from the Italian Medicines Agency was available

METHODS

- This prospective, noninterventional, multicenter CUP was open between January 18, 2021, and March 7, 2022
  - Avelumab 1L maintenance was approved for patients with la/mUC by the European Commission on January 25, 2021[11]
  - Reimbursement for avelumab 1L maintenance has been available in Italy since March 18, 2022
- Inclusion criteria
  - Patients (≥18 years) with unresectable la/mUC (stage IV)
  - No progressive disease after 4-6 cycles of platinum-based chemotherapy
  - Last chemotherapy dose received 4-10 weeks prior to initiation of avelumab maintenance
  - ECOG PS of 0-1
  - Adequate bone marrow, renal, and liver function
  - Not able to participate in any other clinical trial for UC
- Exclusion criteria
  - Prior adjuvant or neoadjuvant systemic therapy within 12 months
  - Prior treatment with an immune checkpoint inhibitor
  - Contraindication to avelumab
- All patients signed an informed consent form before the start of treatment
- Avelumab was provided per physician request and after approval by local ethics committees in accordance with Italian compassionate use regulations[12]
  - Avelumab 800 mg was administered intravenously every 2 weeks per local prescribing information[6]
- Data collected included baseline demographics and disease characteristics, characteristics of 1L chemotherapy, OS, PFS, and safety
- Statistical analysis
  - Descriptive statistics were used to summarize patients' clinical characteristics
  - OS was defined as the time from the start of avelumab to death from any cause and PFS was defined as as the time from the start of avelumab until disease progression or death from any cause, whichever occurred first
  - OS and PFS were estimated using the Kaplan-Meier method from the start of avelumab 1L maintenance; corresponding 95% CIs were calculated

RESULTS

- Between January 2021 and March 2022, 464 patients received avelumab 1L maintenance across 140 Italian centers in the CUP (data cutoff: December 31, 2022)
  - Median follow-up time was 14.6 months (95% CI, 13.9-15.2 months)
- Most patients were male (78.5%), had metastatic disease (74.6%), and had an ECOG PS of 0 (69.2%); the median age was 70.0 years (IQR, 63-76 years; **Table 1**)
- In 66.6% of patients, the primary tumor was in the lower tract; in 31.9% of patients, the primary tumor was in the upper tract
- The 1L platinum-based chemotherapy regimen was carboplatin + gemcitabine in 51.9% of patients and cisplatin + gemcitabine in 46.1%
  - 48.5% of patients had received 4 cycles of platinum-based chemotherapy, 11.6% had received 5 cycles, and 38.2% had received 6 cycles
  - 11.0% of patients had a complete response to 1L chemotherapy, 57.3% had a partial response, and 31.7% had stable disease
- In 386 patients, the median time from the end of 1L chemotherapy to the start of avelumab maintenance was 8.0 weeks (IQR, 6.0-9.0 weeks)
- Median duration of avelumab treatment was 5.3 months (IQR, 2.4-9.1 months)
- At data cutoff, 411 patients were evaluable for OS and PFS
  - Median OS was not reached, with a 12-month OS rate of 69.2% (95% CI, 64.8%-73.7% ; **Figure 1**)
  - Median PFS was 8.1 months (95% CI, 6.1-10.4 months), with a 12-month PFS rate of 44.3% (95% CI, 39.5%-49.1%; **Figure 2**)
- All-cause grade 3/4 adverse events occurred in 33 patients (7.1%)

LIMITATIONS

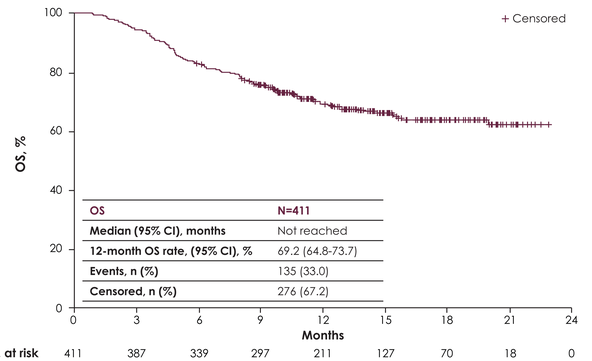
- Safety events may have been underreported because they were reported at the treating physician's discretion
- Short duration of follow-up

Table 1. Patient characteristics at the start of 1L platinum-based chemotherapy

	Patients (N=464)
Age, median (IQR), years	70.0 (63-76)
Sex, n (%)	
Male	364 (78.5)
Female	100 (21.6)
ECOG PS, n (%)	
0	321 (69.2)
1	140 (30.2)
Not reported	3 (0.7)
PD-L1 status, n (%)	
Positive	14 (3.0)
Negative	10 (2.2)
Not reported	440 (94.8)
Disease stage, n (%)	
Metastatic	346 (74.6)
Locally advanced	40 (8.6)
Not reported	78 (16.8)
Site of primary tumor, n (%)	
Lower tract	309 (66.6)
Upper tract	148 (31.9)
Not reported	7 (1.5)
Tumor histology, n (%)	
UC	333 (71.8)
UC with squamous differentiation	26 (5.6)
UC with glandular differentiation	2 (0.4)
UC with variant differentiation	11 (2.4)
Other	7 (1.5)
Not reported	85 (18.3)
Creatinine clearance, n (%)	
>60 mL/min	231 (49.8)
≤60 mL/min	155 (33.4)
Not reported	78 (16.8)
1L chemotherapy regimen, n (%)	
Carboplatin + gemcitabine	241 (51.9)
Cisplatin + gemcitabine	214 (46.1)
MVAC	1 (0.2)
Other	8 (1.7)
No. of 1L chemotherapy cycles, n (%)	
4	225 (48.5)
5	54 (11.6)
6	177 (38.2)
7-9	2 (0.4)
Not reported	6 (1.3)
No. of chemotherapy cycles, median	5
Best response to 1L chemotherapy, n (%)	
Complete response	51 (11.0)
Partial response	266 (57.3)
Stable disease	147 (31.7)

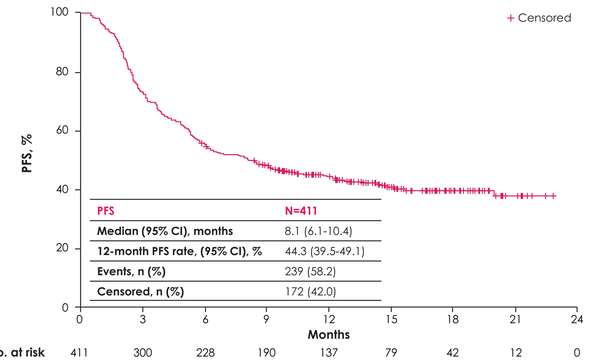
1L, first line; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **MVAC**, methotrexate, vinblastine, doxorubicin, cisplatin; **UC**, urothelial carcinoma.

Figure 1. OS from the start of avelumab 1L maintenance



1L, first line; **OS**, overall survival.

Figure 2. PFS from the start of avelumab 1L maintenance



1L, first line; **PFS**, progression-free survival.

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Please note that this summary contains information from the **full scientific poster presentation**

Avelumab maintenance treatment in people with advanced urothelial cancer in Italy: results from a real-world compassionate use program

View scientific poster

The full title of this poster is: READY: REAl-world Data from an Italian compassionate use program of avelumab first-line maintenance (1LM) treatment for locally advanced or metastatic urothelial carcinoma (la/mUC)

Please note this summary contains information from the scientific poster

'View scientific poster presentation'
(congress registration required)

Date of summary: February 2023

Pronunciations

Medical terms pronunciations

Avelumab <a-VEL-yoo-mab>

Carboplatin <kar-bow-PLA-tin>

Urothelial <YOOR-oh-THEE-lee-ul>

Cisplatin <sis-PLA-tin>

Key takeaways

What are the key takeaways from this summary?

- In the READY study, researchers looked at avelumab maintenance treatment given as a normal clinical treatment for people with advanced urothelial cancer in Italy
- The READY study was a compassionate use program. This means that people could receive avelumab treatment before it became widely available in Italy
- Researchers found that, on average, people treated with avelumab lived for 8 months without their cancer getting worse. They also found that 69% of people were still alive 1 year after starting avelumab
- Overall, the results from this study provide more support for using avelumab as a standard maintenance treatment for people with advanced urothelial cancer

Background

What did this study look at?

What is advanced urothelial cancer?

- Urothelial cancer is a cancer that develops in the urinary tract
- The urinary tract contains the parts of the body that move urine from the kidneys to the outside of the body. It includes:
  - The bladder
  - The inner part of the kidneys
  - Tubes that connect the kidneys to the bladder and the bladder to the outside of the body
- Urothelial cancer is called advanced when it has spread outside of the urinary tract
- Urothelial cancer can spread to nearby tissues or other parts of the body such as bones, lungs, and the liver

How are people with advanced urothelial cancer usually treated?

- Platinum-containing chemotherapy is often the first main treatment given to people with advanced urothelial cancer. This is called first-line treatment
  - Platinum-containing means that the treatment includes a drug that contains platinum (cisplatin or carboplatin)
- Although the cancer may get better with chemotherapy at first, it is likely to start growing again after chemotherapy has ended
- If a person's cancer stops growing or shrinks after first-line chemotherapy, they may then receive avelumab maintenance treatment
  - Maintenance treatment aims to stop the cancer from getting worse or coming back. In other words, it aims to maintain or increase the benefits of first-line treatment

What is avelumab?

Avelumab is a type of immunotherapy. Immunotherapy can help the body's immune system find and destroy cancer cells. Avelumab is given as a drip (infusion) into a vein for about an hour once every 2 weeks

In a previous clinical trial called JAVELIN Bladder 100, researchers found that, on average, people treated with avelumab maintenance treatment + best supportive care lived longer than people who received only best supportive care. Best supportive care includes treatments that help to manage symptoms but do not affect the cancer. A plain language summary of the results is available at **this link**

Avelumab is the only approved first-line maintenance treatment available for people with advanced urothelial cancer that has stopped growing or has shrunk after first-line chemotherapy

What is the READY study?

- The READY study was a compassionate use program that provided avelumab maintenance treatment as a part of normal care for people with advanced urothelial cancer in Italy
- A compassionate use program allows people to receive a treatment before it has become widely available
- In the READY study, people could receive avelumab when the health authority in Italy had yet not started to pay for this treatment
- This compassionate use program was managed by the Italian Medicines Agency
- Information from compassionate use programs helps researchers find out how well a treatment works in a day-to-day setting, outside of a clinical trial
- Everyone taking part in the READY study had received first-line chemotherapy, and their cancer disappeared, shrank, or stopped growing. They then received avelumab first-line maintenance treatment

What did the researchers want to find out?

Researchers wanted to look at results with avelumab maintenance treatment given as part of normal care for people with advanced urothelial cancer in Italy

Study design

What happened during this study?

Who took part in this study?

- From January 2021 to March 2022, 464 people from 140 Italian healthcare centers received avelumab maintenance treatment
- Doctors could request avelumab treatment for any adults with these characteristics:
  - Advanced urothelial cancer
  - Cancer that did not get worse after completing first-line chemotherapy
  - Chemotherapy ended 4 to 16 weeks before the start of avelumab maintenance treatment
- The study plan was approved by ethics committees at all of the healthcare centers
- Researchers analyzed the results in December 2022

Aims of this summary

What did the researchers look at?

Researchers looked at the following:

- Characteristics of people and their cancer before chemotherapy (such as age, sex, and where the cancer started)
- How people were treated with first-line chemotherapy (such as what type was used, how many cycles they received, and what the response was)
- How long people lived after receiving avelumab maintenance
- How long people lived without their cancer getting worse after receiving avelumab maintenance
- How many people had side effects with avelumab maintenance

Results

What were the results of this study?

What were the characteristics of people who took part in the study?

70 years The average age was **70 years**

78% male

22% female

67% had cancer that started in the **lower part of their urinary tract**

32% had cancer that started in the **upper part of their urinary tract**

2% had cancer that started in an **unknown location**

74% had cancer that had **spread to other parts of the body**

9% had cancer that had **spread to nearby tissues only**

17% cancer **spread was not reported**

69% were able to be **fully active**

30% were only able to carry out light work or **less strenuous activity**

1% had **no reported information on activity**

What type of first-line chemotherapy did people receive?

52% received **carboplatin + gemcitabine** chemotherapy

46% received **cisplatin + gemcitabine** chemotherapy

2% received **other types** of chemotherapy

How many cycles of first-line chemotherapy did people receive?

49% received **4 cycles** of chemotherapy

12% received **5 cycles** of chemotherapy

38% received **6 cycles** of chemotherapy

What was the response to first-line chemotherapy (before avelumab treatment)?

11% had cancer that became **undetectable**

57% had cancer that **shrank**

32% had cancer that **stopped growing**

What was the response to avelumab maintenance treatment?

8 MONTHS was the average time that people lived without their cancer getting worse

44% had cancer that remained stable and did not get worse for at least 12 months

69% were still alive for at least 12 months

7% had severe side effects*

*A side effect is considered severe when it limits daily activities such as bathing and dressing, is disabling or medically significant, could be life threatening, needs hospital care, or causes lasting problems.

Conclusions

What were the main conclusions reported by the researchers?

- The real-world READY study showed the characteristics and treatment results of people with advanced urothelial cancer who received avelumab maintenance in Italy as part of a compassionate use program
- Results of this study are similar to the findings of a previous clinical trial
- Overall, the results support the use of avelumab maintenance as a standard treatment for people with advanced urothelial cancer

Disclaimers

Avelumab is approved to treat the condition that is discussed in this summary. This summary reports the results of a single study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study

Study sponsors

Who sponsored this study?

Merck Serono S.p.A., Rome, Italy,
an affiliate of Merck KGaA, Darmstadt, Germany
125 Via Casilina
Rome, 00176, Italy
Phone (Germany): +49 6151 720

Pfizer
235 East 42nd Street
New York, NY 10017, USA
Phone (United States): +1 212-733-2323

The sponsors would like to thank all of the people who took part in this study

More information

Where can I find more information?

For more information on this study, please visit:
2023 ASCO Genitourinary Cancers Symposium Scientific Poster Presentation

For more information on bladder cancer in general, please visit:
https://www.cancer.net/cancer-types/bladder-cancer
https://www.cancer.org/cancer/bladder-cancer.html

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