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Avelumab first-line maintenance for advanced urothelial carcinoma: results from patients with ≥12 months of treatment in JAVELIN Bladder 100

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SCOPE



- We report long-term data from patients who received ≥12 months of avelumab first-line (1L) maintenance treatment in the JAVELIN Bladder 100 trial, which compared avelumab 1L maintenance + best supportive care (BSC; avelumab arm) vs BSC alone (control arm) in patients with advanced urothelial carcinoma (aUC) that had not progressed with 1L platinum-based chemotherapy

CONCLUSIONS



- In the JAVELIN Bladder 100 trial, 33.7% of randomized patients in the avelumab arm received ≥12 months of treatment
 - In this subgroup, median overall survival (OS) was not reached (95% CI, 50.9 months-not estimable [NE]), and median progression-free survival (PFS) was 26.7 months (95% CI, 19.4-32.2)
- Baseline characteristics of patients who received ≥12 months of treatment were generally similar to those of patients in the overall avelumab arm
- Prolonged avelumab 1L maintenance treatment was associated with an acceptable safety profile that was consistent with prior avelumab monotherapy studies,¹ and no new safety signals were identified with longer treatment duration
- These results further support the use of avelumab 1L maintenance until progression or unacceptable toxicity for all patients with aUC that has not progressed with 1L platinum-based chemotherapy

BACKGROUND

- In the phase 3 JAVELIN Bladder 100 trial, avelumab 1L maintenance + BSC significantly prolonged OS and PFS vs BSC alone in patients with aUC that had not progressed with 1L platinum-based chemotherapy²
- Results from this trial led to the approval of avelumab 1L maintenance in various countries worldwide,^{3,4} and it is now recommended as standard of care in international treatment guidelines⁵⁻⁷
- After ≥2 years of follow-up in all patients (data cutoff, 4 June 2021) OS and PFS continued to be prolonged in the avelumab vs control arm⁸
- Median OS was 23.8 vs 15.0 months, respectively (HR, 0.76 [95% CI, 0.631-0.915]; 2-sided p=0.0036)
- Median PFS was 5.5 vs 2.1 months, respectively (HR, 0.54 [95% CI, 0.457-0.645]; 2-sided p<0.0001)
- Avelumab 1L maintenance demonstrated an acceptable long-term safety profile
 - No new safety signals were identified

RESULTS

- At data cutoff (4 June 2021), median follow-up was 38.0 months in the avelumab arm, and all patients had been followed up for ≥2 years
 - 118 of 350 patients (33.7%) had received ≥12 months of treatment
- Baseline characteristics of patients treated for ≥12 months were generally similar to those of patients in the overall avelumab arm (Table 1)

Table 1. Baseline characteristics

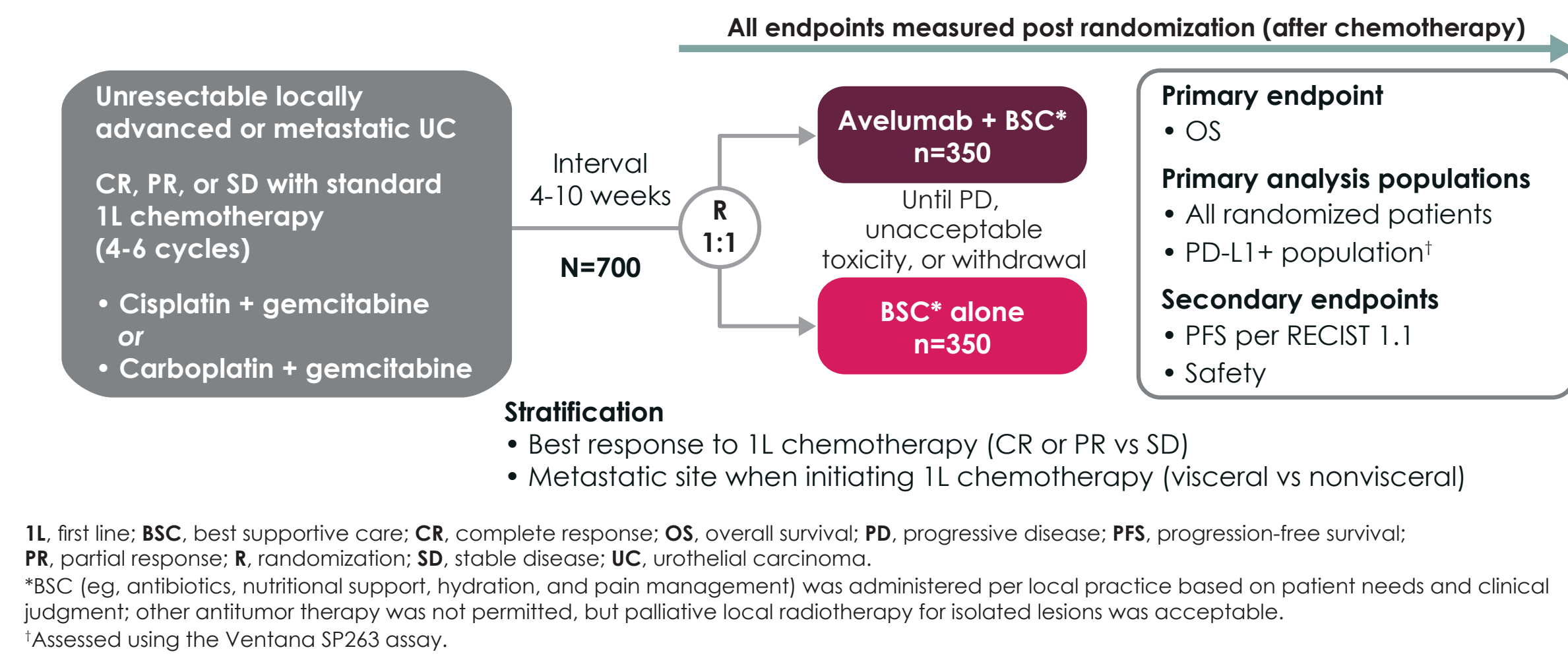
	Overall avelumab arm (N=350)	Patients with ≥12 months of avelumab treatment (n=118)
Age, median (range), years	68 (37-90)	69 (43-86)
Sex, n (%)		
Male	266 (76.0)	91 (77.1)
Female	84 (24.0)	27 (22.9)
Pooled geographic region, n (%)		
Europe	214 (61.1)	61 (51.7)
North America	12 (3.4)	6 (5.1)
Asia	73 (20.9)	32 (27.1)
Australasia	34 (9.7)	15 (12.7)
Rest of the world	17 (4.9)	4 (3.4)
ECOG PS, n (%)		
0	213 (60.9)	83 (70.3)
1	136 (38.9)	35 (29.7)
2	1 (0.3)	0
PD-L1 status, n (%)		
Positive	189 (54.0)	72 (61.0)
Negative	139 (39.7)	39 (33.1)
Unknown	22 (6.3)	7 (5.9)
1L chemotherapy regimen, n (%)		
Gemcitabine + cisplatin	183 (52.3)	67 (56.8)
Gemcitabine + carboplatin	147 (42.0)	43 (36.4)
Gemcitabine + cisplatin + carboplatin*	20 (5.7)	8 (6.8)
Best response to 1L chemotherapy, n (%)		
CR	90 (25.7)	36 (30.5)
PR	163 (46.6)	51 (43.2)
SD	97 (27.7)	31 (26.3)
Site of metastasis at start of chemotherapy, n (%)		
Visceral	191 (54.6)	56 (47.5)
Nonvisceral	159 (45.4)	62 (52.5)
Site of primary tumor, n (%)		
Upper tract	106 (30.3)	34 (28.8)
Lower tract	244 (69.7)	84 (71.2)

1L, first line; CR, complete response; PR, partial response; SD, stable disease.
*Patients who switched platinum regimens while receiving 1L chemotherapy.

METHODS

- JAVELIN Bladder 100 (NCT02603432) enrolled patients with unresectable locally advanced or metastatic UC that had not progressed with 1L platinum-based chemotherapy
- Patients were randomized 1:1 to the avelumab or control arm following an interval of 4-10 weeks from the end of 1L chemotherapy (Figure 1)
- Study treatment continued until disease progression, unacceptable toxicity, or withdrawal of consent
- The primary endpoint was OS, assessed in all randomized patients and in patients with PD-L1+ tumors
- Secondary endpoints included PFS and safety
 - For these long-term follow-up analyses, PFS was based on investigator assessment
- These exploratory analyses include patients who were randomized to the avelumab arm and had received ≥12 months of treatment as part of the trial

Figure 1. JAVELIN Bladder 100 study design²



1L, first line; BSC, best supportive care; CR, complete response; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; R, randomization; SD, stable disease; UC, urothelial carcinoma.
*BSC (eg, antibiotics, nutritional support, hydration, and pain management) was administered per local practice based on patient needs and clinical judgment; other antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable.
†Assessed using the Ventana SP263 assay.

Figure 2. OS in patients with ≥12 months of avelumab treatment

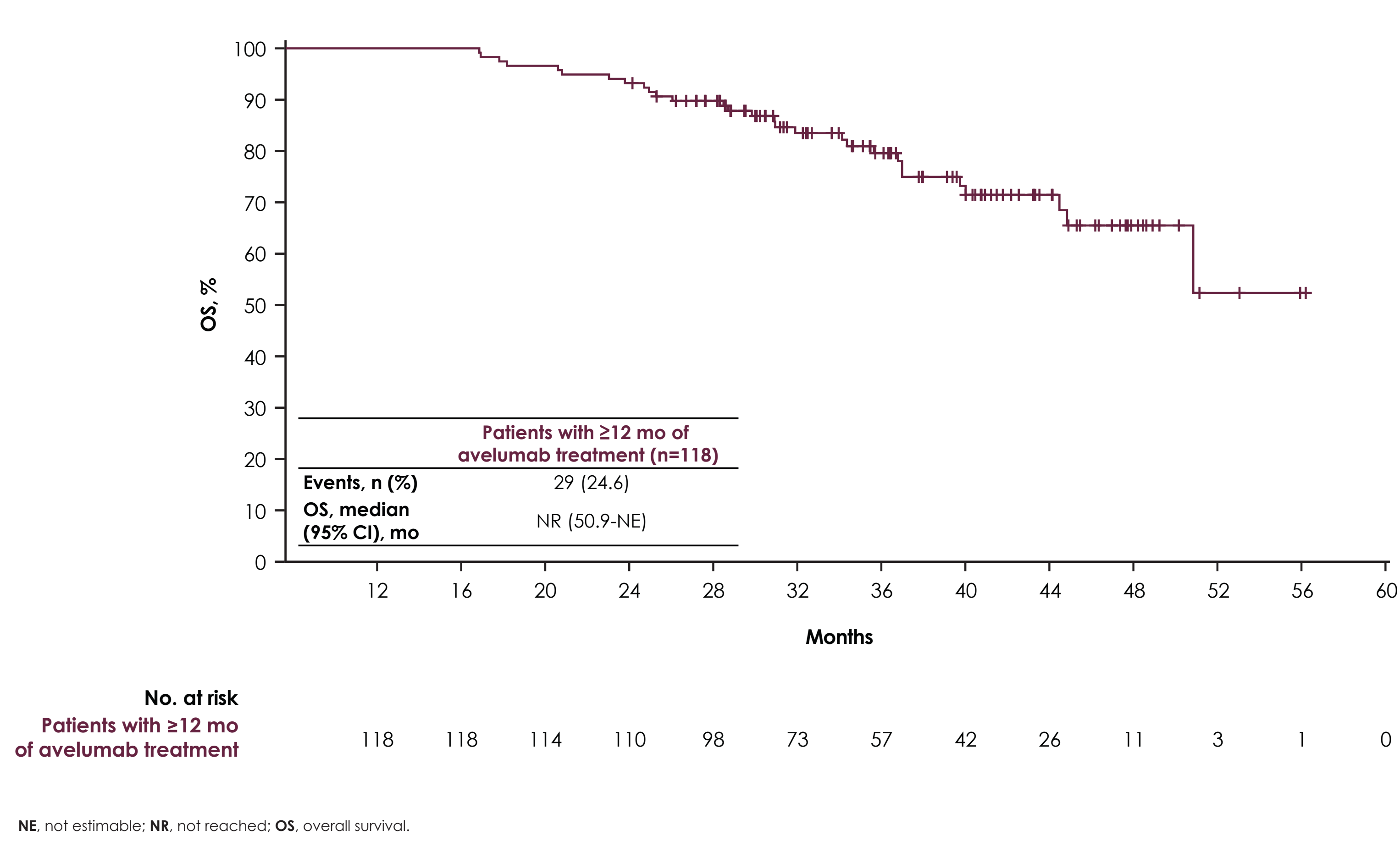
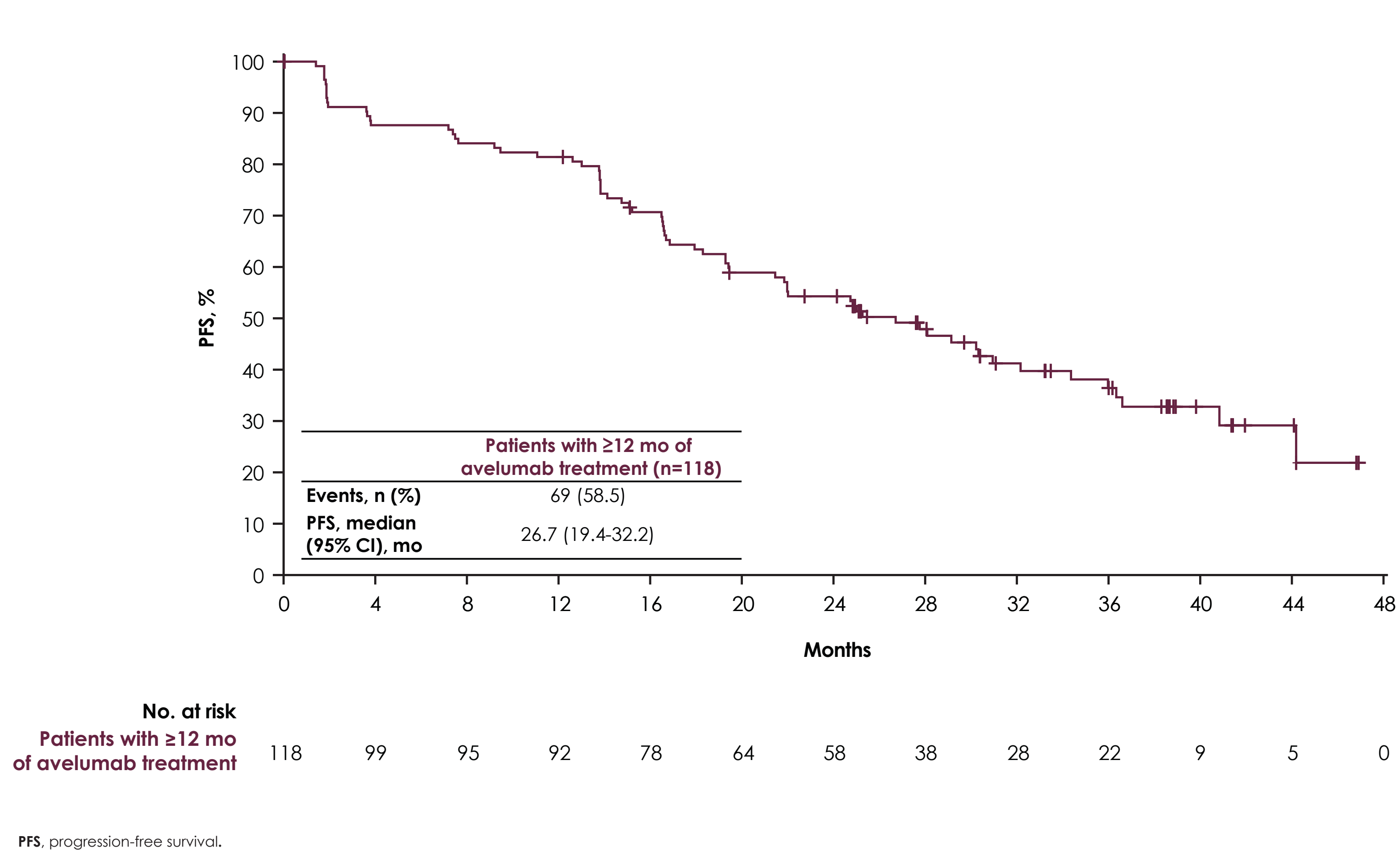


Figure 3. Investigator-assessed PFS in patients with ≥12 months of avelumab treatment



- Among all treated patients in the overall avelumab arm (n=344), any-grade treatment-related adverse events (TRAEs) occurred in 269 patients (78.2%), including grade ≥3 TRAEs in 67 (19.5%) (Table 2)
 - Grade ≥3 immune-related adverse events (irAEs) occurred in 26 patients (7.6%)
- Among patients treated for ≥12 months (n=118), TRAEs of any grade occurred after ≥12 months in 59 patients (50.0%), including grade ≥3 TRAEs in 14 (11.9%) (Table 2)
 - The most common TRAE occurring after ≥12 months of treatment was pruritus (n=13 [11.0%]) (Table 3)
 - Grade ≥3 irAEs occurred after ≥12 months in 5 patients (4.2%; blood creatine phosphokinase increased, colitis, drug eruption [rash], hyperglycemia, and immune-mediated nephritis [n=1 each])

Table 2. Summary of AEs occurring at any time and after ≥12 months of treatment in the avelumab arm

Events, n (%)	Occurred at any time (n=344)*	Occurred after ≥12 months of treatment (n=118)†
AE of any grade	338 (98.3)	102 (86.4)
Grade ≥3 AE	185 (53.8)	56 (47.5)
TRAE of any grade	269 (78.2)	59 (50.0)
Grade ≥3 TRAE	67 (19.5)	14 (11.9)
Serious AE	35 (10.2)	28 (23.7)
Serious TRAE	35 (10.2)	6 (5.1)
AE leading to interruption of avelumab	156 (45.3)	43 (36.4)
AE leading to discontinuation of avelumab	49 (14.2)	13 (11.0)
TRAE leading to discontinuation of avelumab	40 (11.6)	12 (10.2)
AE leading to death	7 (2.0)	3 (2.5)
TRAE leading to death	2 (0.6)	1 (0.8)
irAE of any grade	111 (32.3)	27 (22.9)
Grade ≥3 irAE	26 (7.6)	5 (4.2)

AE, adverse event; irAE, immune-related adverse event; TRAE, treatment-related adverse event.
*All treated patients.
†Patients with ≥12 months of treatment.

Table 3. Most common TRAEs occurring at any time and after ≥12 months of treatment in the avelumab arm

Events, n (%)	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TRAE	269 (78.2)	67 (19.5)	59 (50.0)	14 (11.9)
Pruritus	51 (14.8)	1 (0.3)	13 (11.0)	0
Rash	27 (7.8)	2 (0.6)	8 (6.8)	1 (0.8)
Fatigue	37 (10.8)	1 (0.3)	8 (6.8)	0
Diarrhea	36 (10.5)	0	7 (5.9)	0
Asthenia	36 (10.5)	0	4 (3.4)	0
Lipase increased	15 (4.4)	12 (3.5)	3 (2.5)	2 (1.7)
Hypothyroidism	38 (11.0)	1 (0.3)	3 (2.5)	0
Arthralgia	25 (7.3)	1 (0.3)	3 (2.5)	0
Anemia	14 (4.1)	5 (1.5)	3 (2.5)	0
Nausea	25 (7.3)	1 (0.3)	2 (1.7)	0
Dry skin	18 (5.2)	0	2 (1.7)	0
Infusion-related reaction	34 (9.9)	3 (0.9)	1 (0.8)	0
Amylase increased	15 (4.4)	8 (2.3)	1 (0.8)	0
Chills	24 (7.0)	0	0	0
Pyrexia	23 (6.7)	0	0	0
Hyperthyroidism	21 (6.1)	0	0	0

Table shows TRAEs of any grade occurring in ≥5% of patients or of grade ≥3 occurring in ≥2% of patients.
TRAE, treatment-related adverse event.
*All treated patients.
†Patients with ≥12 months of treatment.

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Results from people with advanced urothelial cancer who had received at least 12 months of avelumab first-line maintenance treatment in the JAVELIN Bladder 100 study

JAVELIN

The full title of this abstract is: Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (aUC): results from patients with ≥12 mo of treatment in JAVELIN Bladder 100

Please note this summary only contains information from the scientific abstract

[View scientific abstract](#)



Date of summary: September 2022

For more information on this study, go to: <https://clinicaltrials.gov/ct2/show/NCT02603432>

Medical terms pronunciations

Avelumab <a-VEL-yoo-mab>

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

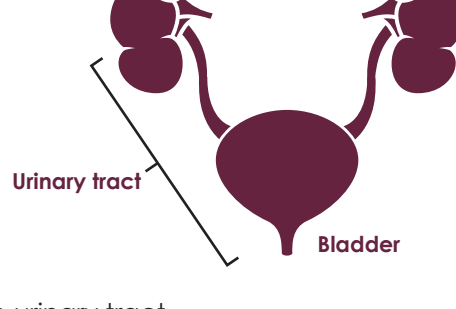
What are the key takeaways from this summary?

- The JAVELIN Bladder 100 study showed that avelumab first-line maintenance treatment, which is given after first-line chemotherapy, helped people with advanced urothelial cancer live longer than people who were not treated with avelumab
 - A plain language summary of the overall results from the JAVELIN Bladder 100 study is available at [this link](#)
- For this summary, researchers looked at people who had received at least 12 months of avelumab first-line maintenance treatment in the JAVELIN Bladder 100 study
 - Researchers found that 34% of people had received at least 12 months of treatment
- The overall safety of long-term avelumab in people who received at least 12 months of treatment was similar to that reported in other studies of avelumab
- Results from this summary provide more support for using avelumab first-line maintenance treatment as a standard treatment for people with advanced urothelial cancer until their cancer gets worse or comes back

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



How is advanced urothelial cancer usually treated?

- Chemotherapy is often the first main treatment given to people with advanced urothelial cancer. This is called first-line treatment
- Although the cancer may get better with chemotherapy at first, it is likely to start growing again
- If a person's cancer stops growing or shrinks after first-line chemotherapy, they may then receive a different treatment. This is called maintenance treatment. It aims to stop the cancer from getting worse or coming back

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
- Results from the JAVELIN Bladder 100 study have shown that avelumab first-line maintenance treatment can help people with advanced urothelial cancer live longer. A plain language summary of the overall results is available at [this link](#)
- Avelumab is the only approved maintenance treatment available for people with advanced urothelial cancer that has stopped growing or shrunk with first-line chemotherapy

What is the JAVELIN Bladder 100 study?

- The JAVELIN Bladder 100 study looked at avelumab first-line maintenance treatment for people with advanced urothelial cancer in various countries worldwide
- All people taking part in the study had received first-line chemotherapy, and their cancer had disappeared, shrunk, or stopped growing. They were put into 2 treatment groups:
 - Treatment group 1 received avelumab first-line maintenance treatment plus best supportive care. Best supportive care includes treatments that help to manage symptoms but do not affect the cancer
 - Treatment group 2 received only best supportive care
- Researchers found that, on average, people who were treated with avelumab plus best supportive care lived longer than people who received only best supportive care
- People continued to receive study treatment until any of the following things happened:
 - Their cancer started growing again
 - They had severe side effects (meaning side effects that limited daily activities such as bathing and dressing, required hospital care, caused lasting problems, or were life threatening)
 - They did not want to take part in the study any more
- Researchers continued to collect information after people stopped receiving study treatment

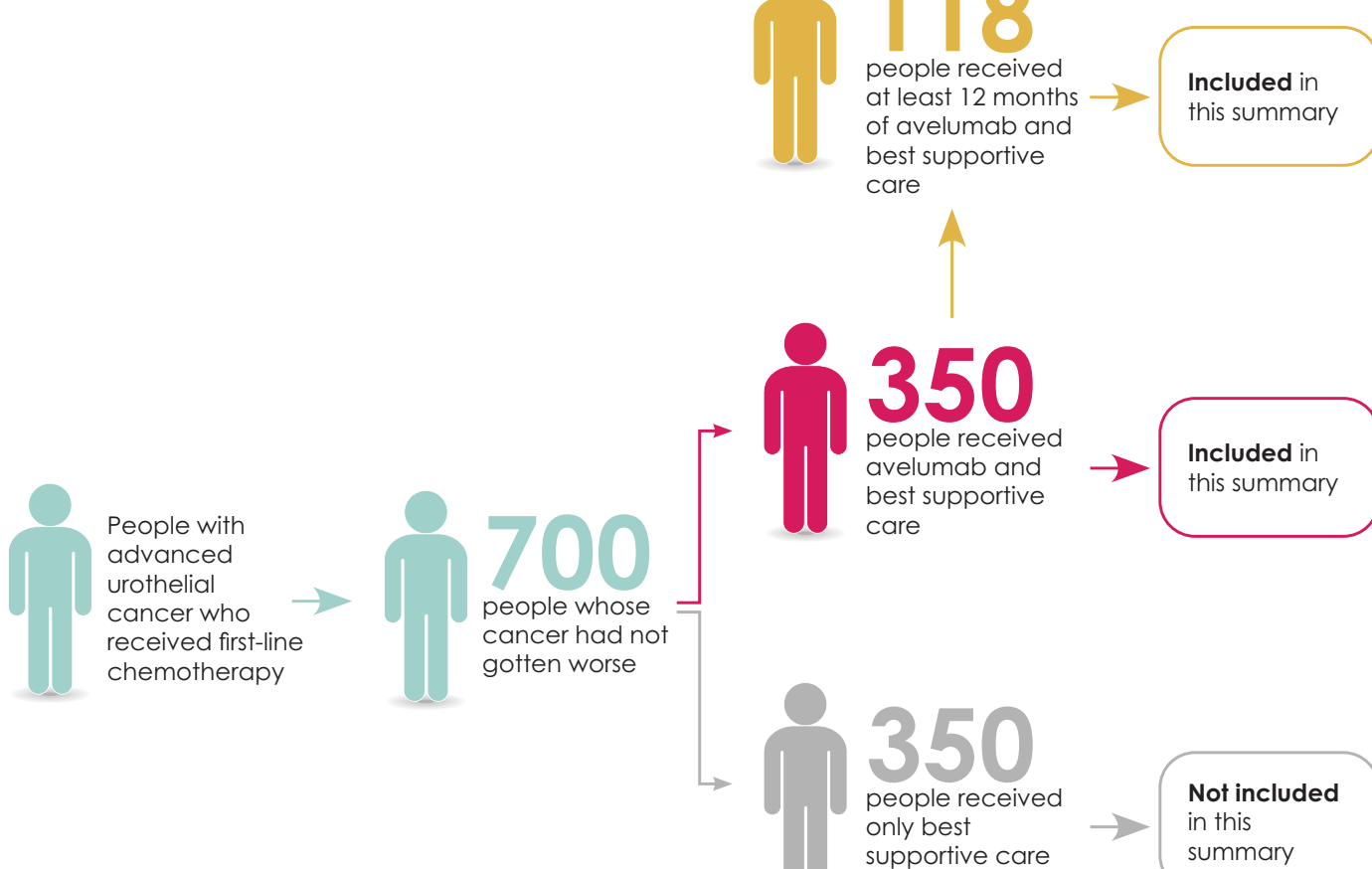
What did the researchers want to find out?

Researchers looked at people who had received avelumab first-line maintenance treatment in the JAVELIN Bladder 100 study. They wanted to look at results in people who had received at least 12 months of avelumab treatment

What happened during the study?

Who took part in the study?

- Researchers looked at all people who had received avelumab and best supportive care in the JAVELIN Bladder 100 study
- For this summary, they looked at people in this treatment group who had received at least 12 months of avelumab first-line maintenance treatment
- On average, people had been studied for 38 months when results were collected. This was in June 2021



What did the researchers look at?

- Researchers looked at the following things in all people who received avelumab and best supportive care and those who received at least 12 months of avelumab first-line maintenance treatment:
 - Characteristics of people before treatment
 - Severe side effects related to avelumab treatment
 - Severe side effects related to avelumab triggering the body's immune system to target normal tissues in the body. These are called immune-related side effects

What were the results of the study?

What were the characteristics of people in each group before they started to receive avelumab and best supportive care?

All people who received avelumab and best supportive care

118 people who received at least 12 months of avelumab and best supportive care

68 years

Average age

69 years

76%

Male

77%

39%

People who were not able to be fully active*

30%

55%

People whose cancer had spread to internal organs

48%

72%

People whose cancer had disappeared or shrunk after chemotherapy

74%

54%

People whose cancer had a protein called PD-L1 on its surface

61%

*Restricted from carrying out strenuous physical activity but able to carry out light work

How many people had severe* side effects?

At any time in all people who received avelumab and best supportive care

After 12 months in the 118 people who received avelumab and best supportive care

20%

People who had severe side effects related to treatment

12%

8%

People who had severe immune-related side effects

4%

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

What were the main conclusions reported by the researchers?

- The characteristics of people who received at least 12 months of avelumab first-line maintenance treatment in the JAVELIN Bladder 100 study were similar to the characteristics of all people who received avelumab first-line maintenance treatment
- Long-term safety results for people who received at least 12 months of avelumab first-line maintenance treatment were similar to what has been seen in other studies of avelumab
 - No new safety concerns were seen with longer treatment length
- Results from this summary provide more support for using avelumab first-line maintenance treatment for people with advanced urothelial cancer until their cancer gets worse or comes back

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. This study described is still ongoing, therefore the final outcomes of this study may differ from the outcomes described in this summary

Who sponsored this study?

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

Where can I find more information?

For more information on this study, please visit:
[ESMO Congress 2022 Scientific Abstract](https://www.clinicaltrials.gov/ct2/show/NCT02603432)
<https://www.clinicaltrials.gov/ct2/show/NCT02603432>

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Writing support for this summary was provided by Jamie Ratcliffe at ClinicalThinking and was funded by Pfizer and Merck (CrossRef Funder ID: 10.13039/100009945)