Long-term outcomes in patients with advanced urothelial carcinoma who received avelumab first-line maintenance with or without second-line treatment: exploratory analyses from JAVELIN Bladder 100

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JAVELIN Bladder 100

SCOPE

- **The JAVELIN Bladder 100 trial showed that avelumab first-line (1L) maintenance + best supportive care (BSC) significantly prolonged overall survival (OS) and progression-free survival (PFS) vs BSC alone in patients with advanced urothelial carcinoma (UC) that had not progressed with 1L platinum-containing chemotherapy[1,2]**
- **We report an exploratory descriptive analysis of outcomes in patients enrolled in the avelumab + BSC arm based on receipt of second-line (2L) treatment**

CONCLUSIONS

- **After long-term follow-up in the avelumab + BSC arm of the JAVELIN Bladder 100 trial (median, 38 months):**
  - **12.3% of patients were still receiving avelumab 1L maintenance**
  - **Approximately 60% of patients who had discontinued avelumab were reported to have received 2L treatment**
- **Long-term OS (in the context of historical data)[3-7] was observed in patients who received avelumab 1L maintenance with or without 2L treatment**
- **The impact of avelumab 1L maintenance on outcomes with 2L therapy remains unknown**
  - **A previous analysis showed that patients in the avelumab 1L maintenance + BSC arm had prolonged time to end of 2L therapy compared with patients in the BSC alone arm (median, 14.8 vs 9.2 months, respectively; hazard ratio [HR], 0.67 [95% CI, 0.545-0.815])[8]**
- **These findings further support avelumab 1L maintenance as standard of care in this treatment setting**

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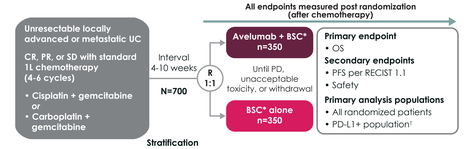
BACKGROUND

- Platinum-containing chemotherapy is standard-of-care 1L treatment for patients with advanced UC[9-11]
  - Median durations of PFS (6-8 months) and OS (12-15 months) for patients who receive 1L platinum-containing chemotherapy without maintenance treatment are short[3-6]
- In the phase 3 JAVELIN Bladder 100 trial, avelumab 1L maintenance therapy + BSC significantly prolonged OS and PFS vs BSC alone in patients with advanced UC that had not progressed with 1L platinum-containing chemotherapy[1,2]
  - With long-term follow-up (median ≥38 months in both arms), OS (measured from randomization, after completion of chemotherapy) and investigator-assessed PFS continued to be prolonged in the avelumab + BSC arm vs the BSC alone arm[2]
  - Median OS was 23.8 vs 15.0 months, respectively (HR, 0.76 [95% CI, 0.63, 0.91]; 2-sided p=0.0036)
  - Median PFS was 5.5 months vs 2.1 months, respectively (HR, 0.54 [95% CI, 0.46-0.64]; 2-sided p<0.001)
- Results from the trial led to the approval of avelumab 1L maintenance in various countries worldwide[12,13]
- The JAVELIN Bladder 100 regimen (avelumab 1L maintenance in patients with advanced UC that has not progressed with 1L platinum-containing chemotherapy) is now recommended as standard of care in international treatment guidelines[9-11]
- Data on outcomes in patients who receive 2L treatment after avelumab 1L maintenance are limited

METHODS

- Patients eligible for the JAVELIN Bladder 100 trial (NCT02603432) had unresectable locally advanced or metastatic UC that had not progressed with 4 to 6 cycles of 1L platinum-containing chemotherapy (gemcitabine + cisplatin or gemcitabine + carboplatin)[1]
- Following an interval of 4 to 10 weeks from the end of 1L chemotherapy, patients were randomized 1:1 to receive avelumab 1L maintenance + BSC or BSC alone (**Figure 1**)
- The primary endpoint was OS
- Exploratory analyses of OS and time from randomization to end of 2L treatment were performed in the avelumab + BSC arm in subgroups defined by 2L treatment administered by investigators after discontinuation of study treatment

Figure 1. JAVELIN Bladder 100 study design[1]



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.

RESULTS

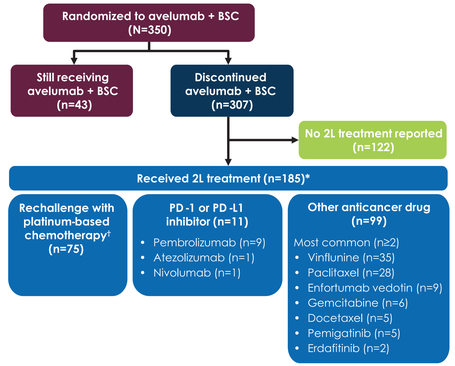
- At data cutoff (June 4, 2021), median follow-up in the avelumab arm was 38.0 months
- **Figure 2** summarizes treatment sequencing for patients in the avelumab arm
  - 43 patients (12.3%) were still receiving avelumab 1L maintenance; median duration of avelumab treatment in this subgroup was 35.6 months (range, 24.5-49.7)
  - 185 patients (52.9%) had discontinued avelumab for any reason and received 2L treatment; median duration of avelumab treatment was 5.1 months (range, 0.5-44.6)
  - 122 patients (34.9%) had discontinued avelumab and did not receive 2L treatment; median duration of avelumab treatment was 5.0 months (range, 0.5-43.7)
- Baseline characteristics were similar between patients in the avelumab arm who did or did not receive 2L treatment (**Table 1**)
- Among patients who received 2L treatment, median time from end of avelumab 1L maintenance to start of 2L treatment was 1.35 months (range, 0.3-30.9)
- Long-term OS (in the context of historical data)[3-7] was observed in patients who received avelumab 1L maintenance and did or did not receive 2L treatment (**Figure 3**)
  - The subgroup of patients who discontinued avelumab with no 2L treatment reported is likely to be heterogenous and may include patients who discontinued avelumab following early disease progression or toxicity in addition to patients who discontinued after experiencing long-term disease control
- Time from randomization to end of 2L treatment by type of 2L treatment administered is shown in **Table 2**

Table 1. Baseline characteristics

	Discontinued avelumab with no 2L treatment reported (n=122)	Discontinued avelumab and received any 2L treatment (n=185)
Age, years		
Median (range)	68.5 (37-90)	69.0 (39-86)
Sex, n (%)		
Male	92 (75.4)	142 (76.8)
Female	30 (24.6)	43 (23.2)
ECOG PS, n (%)		
0	62 (50.8)	122 (65.9)
1	59 (48.4)	63 (34.1)
2	1 (0.8)	0
Race, n (%)		
Asian	26 (21.3)	37 (20.0)
Black or African American	0	2 (1.1)
White	87 (71.3)	121 (65.4)
Other	4 (3.3)	14 (7.6)
Unknown	5 (4.1)	11 (5.9)
Ethnicity, n (%)		
Hispanic or Latino	9 (7.4)	8 (4.3)
Not Hispanic or Latino	102 (83.6)	150 (81.1)
Not reported or unknown	11 (9.0)	27 (14.6)
Site of metastasis at start of 1L chemotherapy, n (%)		
Visceral	61 (50.0)	108 (58.4)
Nonvisceral	61 (50.0)	77 (41.6)
PD-L1 status, n (%)		
Positive	71 (58.2)	89 (48.1)
Negative	44 (36.1)	85 (45.9)
Unknown	7 (5.7)	11 (5.9)
1L chemotherapy regimen, n (%)*		
Gemcitabine + cisplatin	61 (50.0)	94 (50.8)
Gemcitabine + carboplatin	57 (46.7)	80 (43.2)
Best response to 1L chemotherapy, n (%)		
CR	33 (27.0)	45 (24.3)
PR	47 (38.5)	95 (51.4)
SD	42 (34.4)	45 (24.3)

1L, first line; **2L**, second line; **CR**, complete response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PR**, partial response; **SD**, stable disease.
*Patients who switched 1L platinum-based regimens or for whom the 1L platinum-based regimen was not specified are not shown.

Figure 2. Summary of treatment sequencing in the avelumab arm of the JAVELIN Bladder 100 trial



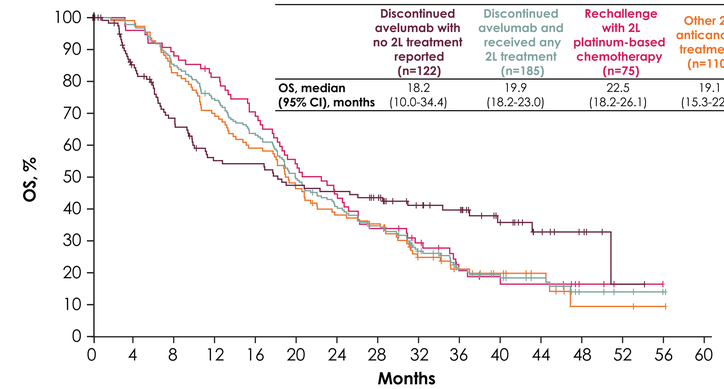
2L, second line; **BSC**, best supportive care.
*Some patients also received third-line or later treatment.
‡Readministration of chemotherapy regimens administered as first-line treatment (cisplatin + gemcitabine or carboplatin + gemcitabine).

Table 2. Time from randomization to end of 2L treatment in the avelumab arm

	N=350	Median time from randomization to end of 2L treatment (95% CI), months
Discontinued avelumab and received any 2L treatment, n (%)	185 (52.9)	11.7 (9.7-13.8)
Rechallenge with 2L platinum-based chemotherapy	75 (21.4)	13.2 (9.3-16.7)
Other 2L anticancer treatment	110 (31.4)	10.8 (8.8-13.0)

Time to end of 2L therapy was defined as the time from the date of randomization to discontinuation of 2L treatment after first objective disease progression by investigator assessment, or death from any cause, whichever occurred first.
2L, second line.

Figure 3. OS in the avelumab arm by type of 2L treatment



No. at risk															
Discontinued avelumab with no 2L treatment reported	122	94	73	57	56	49	47	42	31	27	17	9	5	1	0
Discontinued avelumab and received any 2L treatment	185	181	158	137	117	91	74	60	41	27	19	14	5	3	1	0
Rechallenge with 2L platinum-based chemotherapy	75	72	67	60	52	40	33	25	19	11	8	7	3	1	0
Other 2L anticancer treatment	110	109	91	77	65	51	41	35	22	16	11	7	2	2	1	0

2L, second line; **OS**, overall survival.

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DISCLOSURES J. Bellmunt has served in consulting or advisory roles for Astellas Pharma, AstraZeneca/Medimmune, Bristol Myers Squibb, Genentech, Novartis, Pfizer, Pierre Fabre, and the healthcare business of Merck KGaA, Darmstadt, Germany; has received travel and accommodation expenses from Ipsen, Merck & Co., Kenilworth, NJ, and Pfizer; has received institutional research funding from Millennium, Pfizer/the healthcare business of Merck KGaA, Darmstadt, Germany, and Sanofi; has stock and other ownership interests in Rainier Therapeutics; and has received honoraria from UpToDate. **T. Powles** has served in consulting or advisory roles for Astellas Pharma, AstraZeneca, Bristol Myers Squibb, Eisai, Exelixis, Incyte, Ipsen, Johnson & Johnson, Merck & Co., Kenilworth, NJ, Novartis, Pfizer, Roche, Seattle Genetics, and the healthcare business of Merck KGaA, Darmstadt, Germany; has received travel and accommodation expenses from AstraZeneca, Ipsen, Merck & Co., Kenilworth, NJ, Pfizer, and Roche; and has received institutional research funding from Astellas Pharma, AstraZeneca, Bristol Myers Squibb, Eisai, Exelixis, Ipsen, Johnson & Johnson, Merck & Co., Kenilworth, NJ, Novartis, Pfizer, Pierre Fabre, Roche, Seattle Genetics, and the healthcare business of Merck KGaA, Darmstadt, Germany. **M. Á. Climent Durán** has served in consulting or advisory roles for Astellas Pharma, Bayer, Bristol Myers Squibb, Celgene, Eisai, EUSA Pharma, Janssen-Cilag, Janssen Oncology, Merck and Co., Kenilworth, NJ, Pfizer, Roche/Genentech, Sanofi, and the healthcare business of Merck KGaA, Darmstadt, Germany; has received travel and accommodation expenses from Ipsen, Janssen, Merck and Co., Kenilworth, NJ, Pfizer, and Roche; and has received honoraria from Astellas Pharma, Bayer, Bristol Myers Squibb, EUSA Pharma, Ipsen, Janssen, Merck and Co., Kenilworth, NJ, Novartis, Pfizer, Pierre Fabre, Roche, and Sanofi. **S. S. Sridhar** has served in consulting or advisory roles for Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Immunomedics, Janssen, Merck & Co., Kenilworth, NJ, Pfizer, Roche/Genentech, and Sanofi; and has received institutional research funding from Bayer, Janssen, and Pfizer. **H. Gurney** has served in consulting or advisory roles for AstraZeneca, Bristol Myers Squibb, Ipsen, Janssen-Cilag, Merck & Co., Kenilworth, NJ, Pfizer, Roche, and the healthcare business of Merck KGaA, Darmstadt, Germany; reports speaker services for the healthcare business of Merck KGaA, Darmstadt, Germany; has received travel and accommodation expenses from AstraZeneca. **N. Costa** reports employment by, stock and other ownership interests in, and honoraria from Pfizer. **A. di Pietro** reports employment by and stock and other ownership interests in Pfizer. **B. Huang** reports employment by and stock and other ownership interests in Pfizer. **S. Gupta** has served in consulting or advisory roles for AVEO, Gilead Sciences, Guardant Health, Lava Oncology at Lilly, Merck & Co., Kenilworth, NJ, Pfizer, and the healthcare business of Merck KGaA, Darmstadt, Germany; reports speaker services for Bristol Myers Squibb and Janssen Oncology; has stock and other ownership interests in Moderna Therapeutics and Nektar; and has received honoraria from Bristol Myers Squibb. **P. Grivas** has served in consulting or advisory roles for 4D Pharma PLC, Astellas Pharma, AstraZeneca, Bristol Myers Squibb, Dyania Health, Exelixis, Genentech, Gilead Sciences, Guardant Health, Infinity Pharmaceuticals, Janssen, Merck & Co., Kenilworth, NJ, Mirati Therapeutics, Pfizer, QED Therapeutics, Regeneron Pharmaceuticals, Roche, Seattle Genetics, the healthcare business of Merck KGaA, Darmstadt, Germany, and UroGen; and has received institutional research funding from Bavarian Nordic, Bristol Myers Squibb, Clovis Oncology, Debiopharm Group, G1 Therapeutics, GlaxoSmithKline, Immunomedics, Kure It Cancer Research, Merck & Co., Kenilworth, NJ, Mirati Therapeutics, Pfizer, QED Therapeutics, and the healthcare business of Merck KGaA, Darmstadt, Germany. **ACKNOWLEDGMENTS** This trial is sponsored by Pfizer as part of an alliance between Pfizer and the healthcare business of Merck KGaA, Darmstadt, Germany [CrossRef Funder ID: 10.13039/100009945]. Medical writing support was provided by Jamie Ratcliffe of ClinicalThinking and was funded by Pfizer and the healthcare business of Merck KGaA, Darmstadt, Germany.

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Outcomes in people with advanced urothelial cancer who received different treatments after receiving avelumab in the JAVELIN Bladder 100 study

JAVELIN

The full title of this abstract is: Long-term outcomes in patients with advanced urothelial carcinoma (UC) who received avelumab first-line (1L) maintenance with or without second-line (2L) treatment: Exploratory analyses from JAVELIN Bladder 100

Please note this summary only contains information from the scientific abstract:

View scientific abstract

Date of summary: June 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>

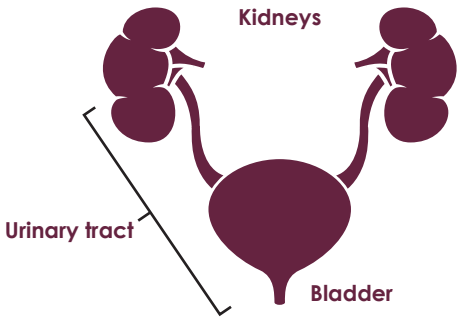
What are the key takeaways from this study?

- The JAVELIN Bladder 100 study showed that avelumab 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 results from the JAVELIN Bladder 100 study is available at this link
- Researchers looked at people who had received avelumab in the JAVELIN Bladder 100 study. In particular, they looked at results in people who did or did not receive a different treatment after they stopped receiving avelumab
- When the results were analyzed, 12% of people were still receiving avelumab
- Among the other 88% of people who had stopped receiving avelumab:
  - 53% had received a different treatment afterward
  - 35% did not receive another treatment
- People treated with avelumab had similar survival times whether or not they had received a different treatment after they stopped receiving avelumab

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



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What did this study look at? (continued)

How is advanced urothelial cancer 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 will usually start growing again
- If a person's cancer stops growing or shrinks with first-line chemotherapy, they may receive a different treatment instead of waiting for the cancer to grow back again. 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 maintenance treatment can help people with advanced urothelial cancer live longer

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 maintenance treatment in 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 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 avelumab

What did the researchers want to find out?

Researchers looked at people who had received avelumab treatment in the JAVELIN Bladder 100 study. They wanted to study long-term outcomes based on whether or not people received a different treatment after stopping avelumab treatment

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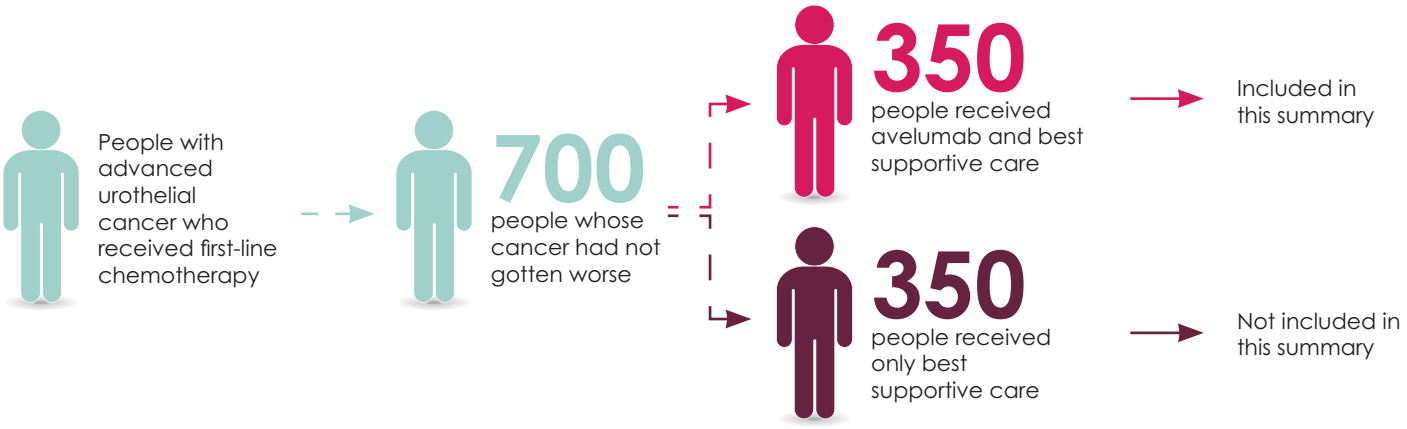
What happened during the study?

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

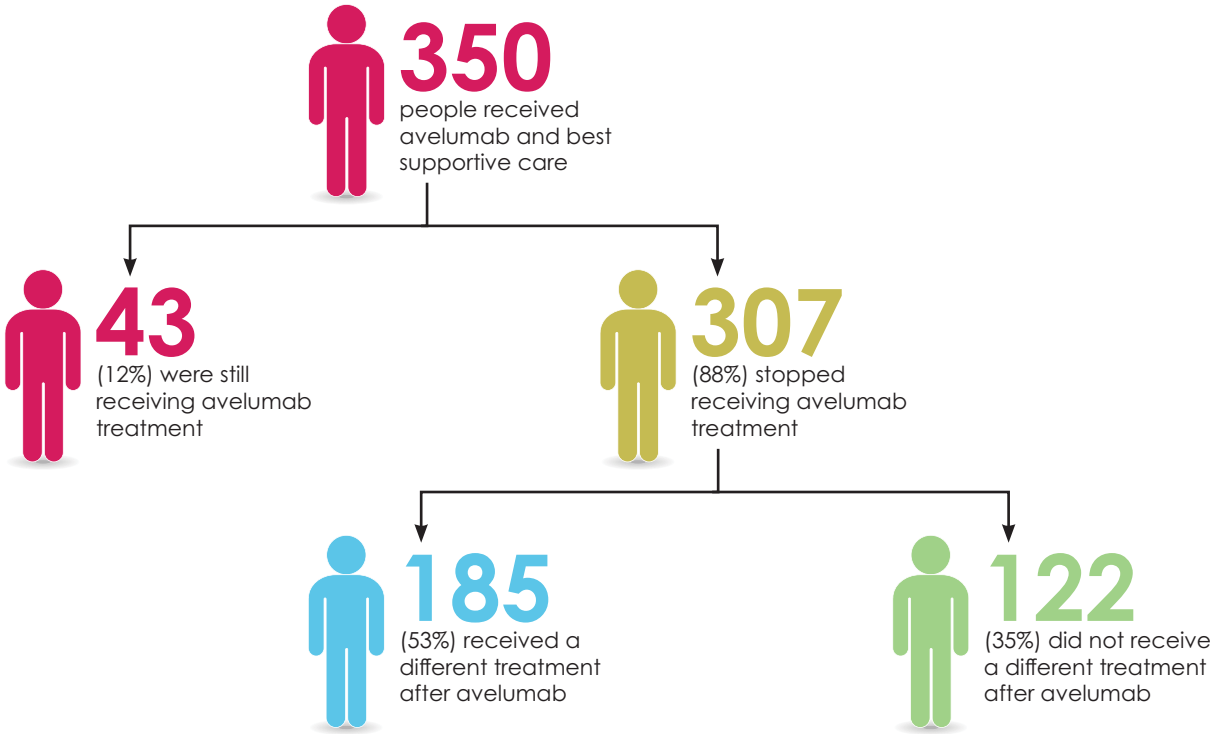


- On average, people had been studied for 38 months when results were collected. This was in June 2021

What did the researchers look at?

- How many people were still receiving avelumab when results were collected
- How many people received a different treatment after stopping avelumab
- How long did people live if they did or did not receive a different treatment after stopping avelumab
- How much time passed between stopping avelumab and starting a different treatment
- Which types of treatment were given after avelumab

What were the results of the study?



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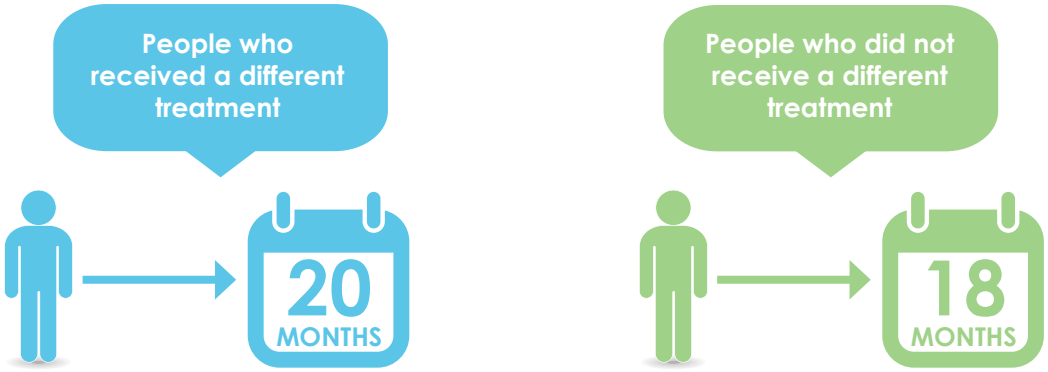
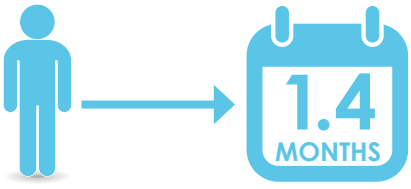
What were the results of the study? (continued)

- On average, the 43 people still receiving avelumab had been treated for 36 months
- 185 out of 307 people who had stopped receiving avelumab received a different treatment afterward

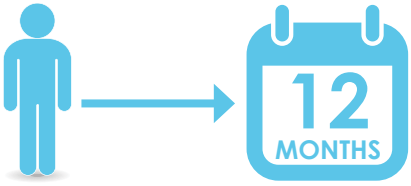
The summary below shows how long at least half of people in the following groups lived after stopping avelumab treatment



The summary below provides more information about people who received a different treatment after stopping avelumab treatment



Average time between stopping avelumab and starting the next treatment



Average time between starting avelumab and stopping the next treatment (or death)

Types of treatments received after stopping avelumab

Repeat chemotherapy
21% of all people who received avelumab

Other treatments
31% of people

including →

Different immunotherapy
3% of people

continued →

What were the main conclusions reported by the researchers?

- In the JAVELIN Bladder 100 study, about 60% of people who stopped avelumab maintenance treatment received a different treatment afterward
- People treated with avelumab had similar survival times whether or not they had received a different treatment after they stopped receiving avelumab

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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Where can I find more information?

For more information on this study, please visit:
2022 ASCO Annual Meeting Scientific Abstract
https://clinicaltrials.gov/ct2/show/NCT02603432

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