Estimated net benefit of avelumab + best supportive care (BSC) vs BSC alone for patients with advanced urothelial carcinoma (aUC) using a quality-adjusted time without cancer symptoms or toxicity (Q-TWiST) analysis

T. Powles,[1] P. Cislo,[2] M. Kirker,[2] J. Chang,[2] N. Gharibian,[2] A. Thompson,[2] N. Costa,[3] P. Grivas[4]

[1]Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, UK; [2]Pfizer, New York, NY, USA; [3]Pfizer, Porto Salvo, Portugal; [4]University of Washington; Fred Hutchinson Cancer Center, Seattle, WA, USA

JAVELIN Bladder 100

SCOPE

- This post hoc analysis of JAVELIN Bladder 100 assessed the net benefit of adding avelumab to BSC in the first-line (1L) maintenance treatment setting after platinum-based chemotherapy in patients with aUC using a Q-TWiST analysis, an integrated measure that incorporates efficacy, safety, and utilities into a single value

CONCLUSIONS

- In this post hoc analysis from the JAVELIN Bladder 100 trial, treatment with avelumab 1L maintenance + BSC resulted in a consistently longer Q-TWiST vs treatment with BSC alone, indicating a net benefit
  - Patients treated with avelumab 1L maintenance + BSC had a greater quality-adjusted time due to delayed disease progression (shorter time after progression or relapse [REL]) and longer overall survival (OS)
- The Q-TWiST benefit reflects the safety profile of avelumab 1L maintenance in the context of a survival benefit
  - These results further support the use of avelumab 1L maintenance as a standard treatment for patients with aUC without disease progression following 1L platinum-based chemotherapy

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Correspondence: **Thomas Powles**, thomas.powles1@nhs.net

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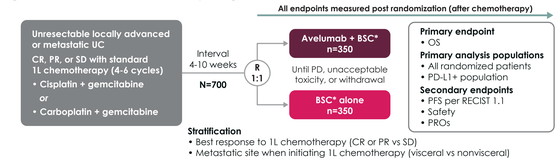
BACKGROUND

- In the phase 3 JAVELIN Bladder 100 trial, avelumab 1L maintenance + BSC significantly prolonged OS and progression-free survival (PFS) vs BSC alone in patients with aUC without progression following 1L platinum-based chemotherapy[1]
  - After ≥2 years of follow-up in all patients, median OS was 23.8 vs 15.0 months, respectively (hazard ratio [HR], 0.76 [95% CI, 0.63-0.91]; 2-sided p=0.0036)[2]
  - Median PFS was 5.5 vs 2.1 months , respectively (HR, 0.54 [95% CI, 0.46-0.64]; 2-sided p<0.0001)[2]
  - The safety profile of avelumab 1L maintenance was consistent with that of prior studies, with no new safety signals identified[1,2]
  - Analysis of patient-reported outcomes (secondary endpoint) showed that the addition of avelumab to BSC did not have a detrimental impact on quality of life[3]
- The Q-TWiST analysis is an integrated measure that incorporates efficacy (ie, OS, PFS), safety (ie, toxicity), and utility estimates (ie, overall health status) into a single value to demonstrate quality and quantity of observed survival time[4,5]
  - The Q-TWiST value contextualizes the clinical benefit of extended life and delay in progression by accounting for the impact on quality of life due to toxicity and disease progression
  - When comparing an intervention with the control arm, a positive between-treatment difference in Q-TWiST represents a net benefit for the intervention
- We report a post hoc Q-TWiST analysis using data from the JAVELIN Bladder 100 trial

METHODS

- The phase 3 JAVELIN Bladder 100 trial (NCT02603432) enrolled patients with unresectable locally advanced or metastatic UC without progression after 1L platinum-based chemotherapy (cisplatin + gemcitabine or carboplatin + gemcitabine)
- Patients were randomized 1:1 to receive avelumab 1L maintenance + BSC or BSC alone (**Figure 1**)
- Treatment continued until confirmed disease progression, unacceptable toxicity, or withdrawal of consent
- The primary endpoint was OS, and secondary endpoints included safety and patient-reported outcomes
- Data cutoff was June 4, 2021 (≥2 years of follow-up in all patients)
- Mean OS was partitioned into 3 health states:
  - Time experiencing toxicity (TOX) prior to progression
  - Time without toxicity or symptoms of disease progression (TWiST)
  - Time after progression or relapse (REL)
- In this analysis, all-cause grade 3/4 toxicities were included
- To ensure equal observation time for each arm, analysis time was restricted to a period of 47.7 months from randomization, which was the shorter follow-up time between arms
- A threshold analysis was conducted using a hypothetical range of utility values typically reported in similar analyses, as well as a range of utility scores estimated from JAVELIN Bladder 100
  - The time in each health state was weighted by utilities and then summed to estimate Q-TWiST to account for differences in quality of life
  - Mean between-treatment differences for each health state were calculated
  - Bootstrap methods were used to estimate CIs for means and difference between means

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; **PRO**, patient-reported outcome; **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.

RESULTS

- Time in TOX was slightly longer with avelumab + BSC vs BSC alone; however, time spent in TWiST was much longer with avelumab + BSC (**Table 1**)
- Time in REL was shorter with avelumab + BSC vs BSC alone because patients in the avelumab + BSC arm spent more time in a progression-free state, which led to less time in REL (**Table 1**)
- Average times spent in each health state are shown in **Figure 2**
  - The area representing TWiST is larger for avelumab + BSC vs BSC alone
- The threshold utility analysis using a range of hypothetical utilities to weight the health states is shown in **Table 2**
  - The difference in Q-TWiST ranged from a maximum of 7.07 (weight for TOX, 1; weight for REL, 0) to a minimum of 3.72 (weight for TOX, 0; weight for REL, 1)
    - The first scenario demonstrates a case in which a patient's quality of life before progression is unaffected by toxicity, but quality of life after progression is severely affected
    - The second scenario demonstrates the opposite case, in which a patient's quality of life before progression is severely affected, but quality of life after progression is unaffected
- The threshold utility analysis using utility weights estimated from JAVELIN Bladder 100 is shown in **Table 3**
- Irrespective of the range of utility values explored for each health state, the Q-TWiST estimate was always longer with avelumab + BSC vs BSC alone (**Table 2** and **Table 3**)

Table 1. Restricted health state durations

Mean (95% CI), months	Avelumab + BSC (n=350)	BSC alone (n=350)	Mean difference (avelumab + BSC – BSC alone)
TOX	1.81 (1.346, 2.196)	1.19 (0.761, 1.602)	0.61 (−0.013, 1.204)
TWiST	11.98 (10.722, 13.202)	5.52 (4.516, 6.530)	6.46 (4.824, 8.194)
REL	12.99 (11.821, 14.087)	15.72 (14.495, 16.993)	−2.74 (−4.593, −1.115)
PFS	13.79 (12.446, 15.102)	6.71 (5.771, 7.631)	7.07 (5.367, 8.802)
OS	26.77 (25.384, 28.165)	22.44 (21.089, 23.758)	4.34 (2.398, 6.236)

Progression data are based on investigator assessment.
BSC, best supportive care; **OS**, overall survival; **PFS**, progression-free survival; **REL**, time after progression or relapse; **TOX**, time experiencing toxicity; **TWiST**, time without toxicity or symptoms of disease progression.

Table 2. Threshold utility analysis using hypothetical ranges of utility scores

TOX weight	TWiST weight	REL weight	Expected Q-TWiST difference* (95% CI)
0	1	0	6.46 (4.824, 8.194)
0	1	0.25	5.78 (4.276, 7.376)
0	1	0.5	5.09 (3.573, 6.676)
0	1	0.75	4.41 (2.742, 6.104)
0	1	1	3.72 (1.806, 5.661)
0.25	1	0	6.61 (4.951, 8.324)
0.25	1	0.25	5.93 (4.420, 7.516)
0.25	1	0.5	5.25 (3.718, 6.822)
0.25	1	0.75	4.56 (2.863, 6.225)
0.25	1	1	3.88 (1.986, 5.802)
0.5	1	0	6.77 (5.129, 8.439)
0.5	1	0.25	6.08 (4.569, 7.650)
0.5	1	0.5	5.40 (3.835, 7.013)
0.5	1	0.75	4.71 (3.005, 6.390)
0.5	1	1	4.03 (2.148, 5.962)
0.75	1	0	6.92 (5.279, 8.590)
0.75	1	0.25	6.24 (4.685, 7.843)
0.75	1	0.5	5.55 (3.971, 7.192)
0.75	1	0.75	4.87 (3.155, 6.557)
0.75	1	1	4.18 (2.256, 6.087)
1	1	0	7.07 (5.367, 8.802)
1	1	0.25	6.39 (4.744, 8.025)
1	1	0.5	5.71 (4.045, 7.332)
1	1	0.75	5.02 (3.265, 6.725)
1	1	1	4.34 (2.398, 6.236)

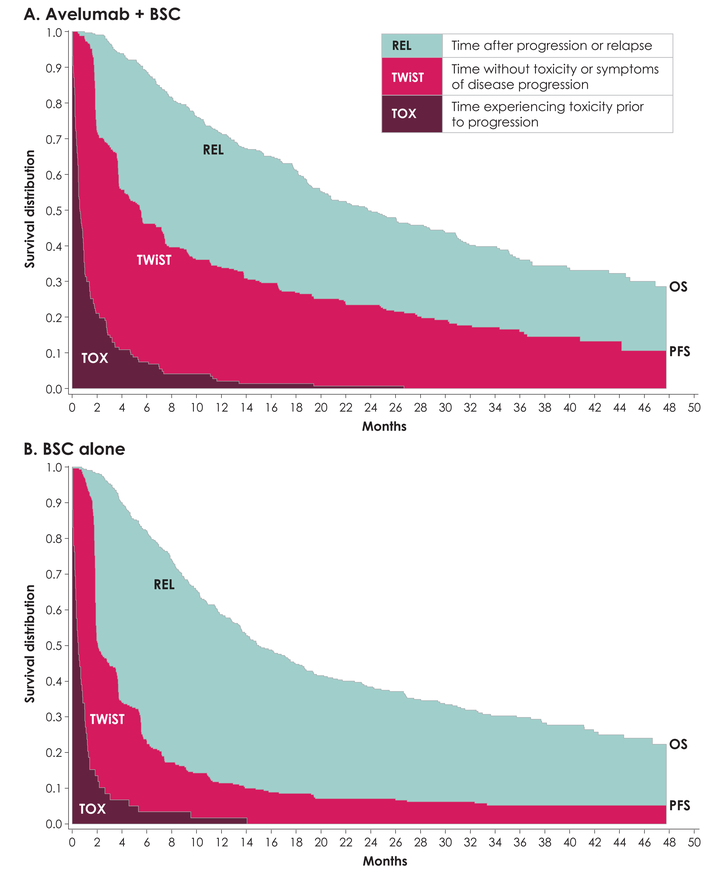
BSC, best supportive care; **Q-TWiST**, quality-adjusted time without cancer symptoms or toxicity; **REL**, time after progression or relapse; **TOX**, time experiencing toxicity; **TWiST**, time without toxicity or symptoms of disease progression.
*Q-TWiST difference between the avelumab + BSC and BSC alone arms in favor of avelumab + BSC.

Table 3. Threshold utility analysis using estimated JAVELIN Bladder 100 utility scores

TOX weight	TWiST weight	REL weight	Expected Q-TWiST difference* (95% CI)
0.5211	0.7883	0.687	3.53 (2.118, 4.937)
0.5211	0.7883	0.701	3.49 (2.058, 4.915)
0.5211	0.7883	0.714	3.46 (2.013, 4.883)
0.5211	0.8030	0.687	3.63 (2.201, 5.046)
0.5211	0.8030	0.701	3.59 (2.147, 5.021)
0.5211	0.8030	0.714	3.55 (2.096, 5.000)
0.5211	0.8174	0.687	3.72 (2.286, 5.158)
0.5211	0.8174	0.701	3.68 (2.233, 5.126)
0.5211	0.8174	0.714	3.65 (2.183, 5.103)
0.5986	0.7883	0.687	3.58 (2.157, 4.996)
0.5986	0.7883	0.701	3.54 (2.103, 4.964)
0.5986	0.7883	0.714	3.51 (2.054, 4.940)
0.5986	0.8030	0.687	3.67 (2.233, 5.103)
0.5986	0.8030	0.701	3.64 (2.185, 5.075)
0.5986	0.8030	0.714	3.60 (2.136, 5.050)
0.5986	0.8174	0.687	3.77 (2.312, 5.209)
0.5986	0.8174	0.701	3.73 (2.262, 5.181)
0.5986	0.8174	0.714	3.69 (2.216, 5.158)
0.6778	0.7883	0.687	3.63 (2.203, 5.049)
0.6778	0.7883	0.701	3.59 (2.151, 5.028)
0.6778	0.7883	0.714	3.55 (2.104, 5.006)
0.6778	0.8030	0.687	3.72 (2.278, 5.162)
0.6778	0.8030	0.701	3.69 (2.234, 5.136)
0.6778	0.8030	0.714	3.65 (2.184, 5.111)
0.6778	0.8174	0.687	3.82 (2.352, 5.271)
0.6778	0.8174	0.701	3.78 (2.307, 5.245)
0.6778	0.8174	0.714	3.74 (2.265, 5.222)

BSC, best supportive care; **Q-TWiST**, quality-adjusted time without cancer symptoms or toxicity; **REL**, time after progression or relapse; **TOX**, time experiencing toxicity; **TWiST**, time without toxicity or symptoms of disease progression.
*Q-TWiST difference between the avelumab + BSC and BSC alone arms in favor of avelumab + BSC.

Figure 2. Partitioned survival plots of TOX, TWiST, and REL for avelumab + BSC and BSC alone based on Kaplan-Meier analysis. In each figure, the OS curve (top line) is partitioned by curves for PFS (middle line) and TOX (bottom line). The area between the curves illustrates the time in each of the 3 health states in the Q-TWiST analysis: REL, TWiST, and TOX



REL	Time after progression or relapse
TWiST	Time without toxicity or symptoms of disease progression
TOX	Time experiencing toxicity prior to progression

BSC, best supportive care; **OS**, overall survival; **PFS**, progression-free survival; **Q-TWiST**, quality-adjusted time without cancer symptoms or toxicity.

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Please note that this summary contains information from the full scientific abstract

Benefit of avelumab and best supportive care vs only best supportive care regarding time without cancer symptoms or side effects in people with advanced urothelial cancer

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The full title of this poster is: Estimated net benefit of avelumab (AVE) + best supportive care (BSC) vs BSC alone for patients (pts) with advanced urothelial carcinoma (aUC) using a quality-adjusted time without cancer symptoms or toxicity (Q-TWiST) analysis

Please note this summary only contains information from the scientific abstract

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Date of summary: June 2023

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

Pronunciations

Medical terms pronunciations

Avelumab <a-VEL-yoo-mab>

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

Key takeaways

What are the key takeaways from this summary?

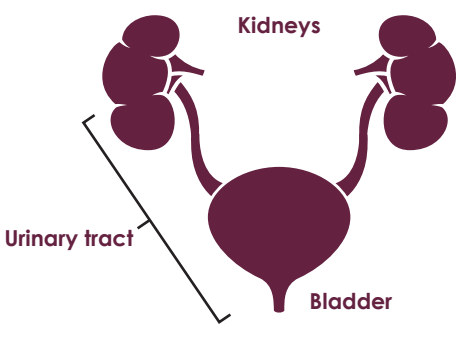
- A study called JAVELIN Bladder 100 showed that avelumab maintenance treatment helped people with advanced urothelial cancer live longer than people who did not receive this treatment
  - Avelumab was given to people whose cancer had disappeared, shrank, or stopped growing with first-line chemotherapy
  - The study also showed that receiving avelumab maintenance treatment did not affect people's quality of life
- Findings from this study led to avelumab maintenance treatment becoming a standard treatment for people with advanced urothelial cancer
- A plain language summary of the overall results from the JAVELIN Bladder 100 study is available at this link
- In this follow-up analysis from the JAVELIN Bladder 100 study, researchers looked at how long people lived without cancer symptoms or severe side effects after starting either avelumab maintenance treatment and best supportive care or only best supportive care
  - This analysis looked at treatment benefits by combining several measures, including cancer assessments, treatment outcomes, side effects, and symptoms reported by people who received treatment
  - Researchers call this type of analysis "quality-adjusted time without cancer symptoms or toxicity," or Q-TWiST for short
- Researchers found that people who received avelumab maintenance treatment lived about 6 months longer without either cancer symptoms or severe side effects than those who received only best supportive care
  - People who received avelumab maintenance treatment also lived longer without their cancer getting worse
- Overall, these results provide more support for using avelumab maintenance as a standard 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?

- Chemotherapy is often the first 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 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

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 first-line maintenance treatment available for people with advanced urothelial cancer that has stopped growing or shrunk after 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 many countries worldwide
- People who took part in the study had received first-line chemotherapy, and their cancer had disappeared, shrank, or stopped growing. They were randomly put into 2 treatment groups:
  - 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
  - Group 2 received only best supportive care

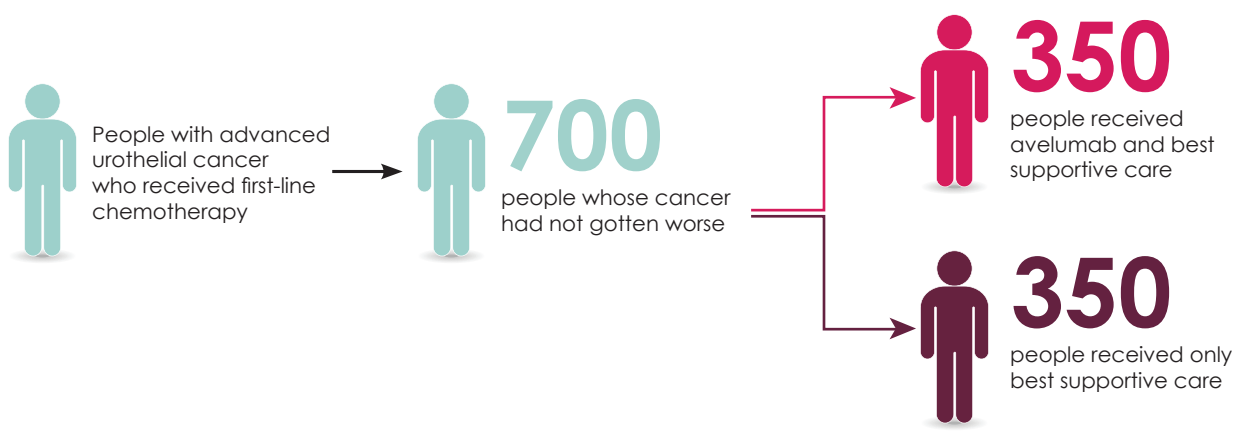
What did the researchers want to find out in this analysis?

In this follow-up analysis from the JAVELIN Bladder 100 study, researchers compared treatment outcomes with avelumab maintenance and best supportive care vs only best supportive care in people with advanced urothelial cancer by combining different measures. These included cancer assessments, treatment outcomes, side effects, and symptoms reported by people who received treatment

Study design

What happened during this analysis?

Who took part in this analysis?



Aims of this summary

What did the researchers look at for this summary?

- How long people lived without either severe side effects or symptoms of cancer
  - A side effect is called severe if it needs urgent treatment, needs or lengthens hospital care, limits self-care, or is disabling or life-threatening
- How long people lived with severe side effects
- How long people lived without their cancer getting worse
- How long people lived after their cancer got worse
- How long people lived overall

Results

What were the results of this analysis?

How long did people in each group live, in general…	Avelumab and best supportive care	Only best supportive care
– without either severe side effects or symptoms of cancer?	12 MONTHS	6 MONTHS
– with severe side effects	2 MONTHS	1 MONTHS
– without their cancer getting worse?	14 MONTHS	7 MONTHS
– after their cancer had got worse?	13 MONTHS	16 MONTHS

Conclusions

What were the main conclusions reported by the researchers?

- In the JAVELIN Bladder 100 study, people with advanced urothelial cancer who received avelumab maintenance treatment and best supportive care lived longer without cancer symptoms or severe side effects than people who received only best supportive care
- In this follow-up analysis, people who received avelumab maintenance treatment and best supportive care lived longer until their cancer got worse, and lived longer overall compared to people who received only best supportive care
- These results showed the safety profile and survival benefits of avelumab maintenance treatment

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

Study sponsors

Who sponsored this study?

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

The healthcare business of Merck KGaA, Darmstadt, Germany
Frankfurter Strasse 250
Darmstadt, 64293, Germany
Phone (Germany): +49 6151 720

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More information

Where can I find more information?

For more information on this study, please visit:
ASCO 2023 Annual Meeting Scientific Abstract
https://clinicaltrials.gov/ct2/show/NCT02603432

For more information on bladder cancer in general, please visit:
https://www.clinicaltrials.gov/ct2/about-studies/learn
https://www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html

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