JAVELIN Bladder Medley: a phase 2 trial of avelumab in combination with other antitumor drugs as first-line maintenance therapy for advanced urothelial carcinoma

J. Hoffman-Censits,[1] P. Grivas,[2] T. Powles,[3] D. Martincic,[4] J. Hawley,[2] K. Tyroller,[5] S. Seeberger,[6] S. Guenther,[7] N. Jacob,[8] K. Tadjalli Mehr,[8] N. Hahn[9]

[1]Departments of Medical Oncology and Urology, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins Medical Institutions, Baltimore, MD, USA; [2]University of Washington, Fred Hutchinson Cancer Center, Seattle, WA, USA; [3]Department of Genitourinary Oncology, Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, UK; [4]Beacon Cancer Care, Coeur d'Alene, ID, USA; [5]R&D Global Biostatistics, Epidemiology & Medical Writing, EMD Serono, Billerica, MA, USA; [6]Global Patient Safety-Medical Safety, the healthcare business of Merck KGaA, Darmstadt, Germany; [7]Global Medical Affairs, the healthcare business of Merck KGaA, Darmstadt, Germany; [8]Global Clinical Development, the healthcare business of Merck KGaA, Darmstadt, Germany; [9]Oncology and Urology, Johns Hopkins University, Johns Hopkins Greenberg Bladder Cancer Institute, Baltimore, MD, USA

JAVELIN Bladder Medley

SCOPE

- **The objective of the phase 2, multicenter, randomized, open-label, parallel-arm JAVELIN Bladder Medley umbrella trial (NCT05327530) is to assess the safety and efficacy of avelumab in combination with other antitumor agents as first-line (1L) maintenance treatment for patients with advanced urothelial carcinoma (UC)**
- **JAVELIN Bladder Medley will show whether 1L maintenance treatment with avelumab-based combinations can improve progression-free survival (PFS) vs avelumab alone**

STUDY STATUS

- **The trial opened in June 2022, and enrollment has begun**
- **The estimated primary completion date is August 2026**
- **For more information, please visit https://clinicaltrials.gov/ct2/show/NCT05327530**

ClinicalTrials.gov record

GET POSTER PDF

Copies of this poster obtained through this quick response (QR) code are for personal use only and may not be reproduced without permission from SITC and the author of this poster

Correspondence: **Jean Hoffman-Censits, jhoffm57@jhmi.edu**

GET PLAIN LANGUAGE SUMMARY

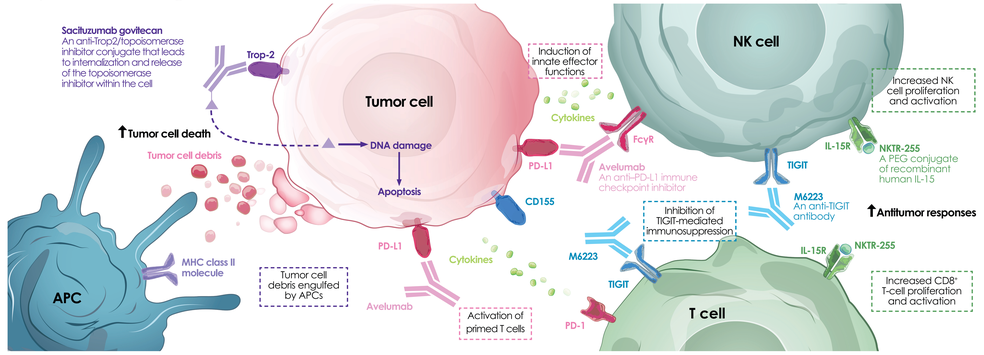
Please scan this quick response (QR) code with your smartphone app to view a plain language summary of the accepted scientific abstract

BACKGROUND

- Bladder cancer, which accounts for >90% of cases of UC,[1] is the 10th most common cancer worldwide[2]
- In the JAVELIN Bladder 100 phase 3 trial (NCT02603432), avelumab (anti–PD-L1 immune checkpoint inhibitor) 1L maintenance + best supportive care (BSC) significantly prolonged overall survival (OS) and PFS vs BSC alone in patients with advanced UC that had not progressed with 1L platinum-containing chemotherapy[3]
  - After ≥2 years of follow-up in all patients, 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]; 2-sided p=0.0036)
  - Median PFS by investigator was 5.5 vs 2.1 months, respectively (HR, 0.54 [95% CI, 0.457-0.645]; 2-sided p<0.0001)
  - Kaplan-Meier curves for OS and PFS are available in the Enhanced Content (QR code)
- Results from JAVELIN Bladder 100 provided level 1 evidence to establish avelumab 1L maintenance as the standard of care for patients with advanced UC that has not progressed with 1L platinum-containing chemotherapy in international treatment guidelines[1,4,5]
- 1L maintenance treatment with avelumab in combination with other antitumor agents targeting different pathways has the potential to provide increased efficacy compared with avelumab alone
- The JAVELIN Bladder Medley trial is investigating the combination of avelumab with 3 other agents as 1L maintenance treatment

Enhanced content

Study rationale: combining avelumab with sacituzumab govitecan, M6223, or NKTR-255 aims to increase antitumor activity[6-13]



APC, antigen-presenting cell; **IL**, interleukin; **IL-15R**, IL-15 receptor; **MHC**, major histocompatibility complex; **NK**, natural killer; **PEG**, polyethylene glycol; **TIGIT**, T-cell immunoreceptor with immunoglobulin and ITIM domains.

KEY ELIGIBILITY CRITERIA

Key inclusion criteria

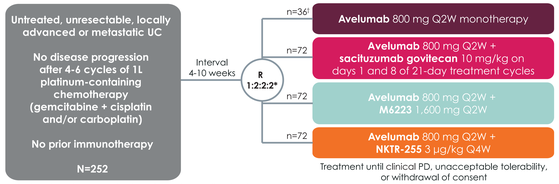
- Age ≥18 years
- Histologically confirmed, unresectable, locally advanced or metastatic UC (stage IIIA/IIIB with N1-N3, or stage IV disease at the start of 1L chemotherapy)
  - Both transitional cell and mixed transitional/nontransitional cell histologies are allowed, but transitional cell carcinoma must be the predominant histology
- No disease progression (per RECIST 1.1) following 4-6 cycles of 1L platinum-containing chemotherapy (gemcitabine + cisplatin and/or carboplatin)
- Last dose of 1L chemotherapy received 4-10 weeks prior to randomization
- Archival or fresh tumor sample available
- ECOG PS 0-1
- Adequate bone marrow, renal, and liver function

Key exclusion criteria

- Prior treatment with immunotherapy, anti-Trop2 agents, any other antibody or drug targeting T-cell costimulation or immune checkpoint pathways, or any of the investigational drugs to be used in combination with avelumab

1L, first line; **UC**, urothelial carcinoma.

JAVELIN BLADDER MEDLEY STUDY DESIGN



The first 21 patients will be randomized in a safety run-in phase (3 patients in the avelumab monotherapy group and 6 patients in each combination group).
1L, first line; **Q2W**, every 2 weeks; **Q4W**, every 4 weeks; **PD**, progressive disease; **R**, randomization; **UC**, urothelial carcinoma.
*Stratified based on the presence or absence of visceral metastases at the start of 1L chemotherapy.
†The control group of 36 randomized patients is planned to be extended using data from an external source, ie, the JAVELIN Bladder 100 trial.[14]

ENDPOINTS

Primary endpoints

- **PFS:** time from randomization to progressive disease according to RECIST 1.1 per investigator assessment, or death
- **Safety and tolerability of the combinations:** occurrence of treatment-emergent AEs, treatment-related AEs, and AEs of special interest throughout the study in all patients who have received ≥1 dose of study treatment

Secondary endpoints

- **OS:** time from randomization to death
- **Objective response** according to RECIST 1.1 per investigator assessment
- **Duration of response:** time from first documentation of objective response to progressive disease or death, according to RECIST 1.1 per investigator assessment
- **PK:** study drug concentration, population PK analyses, and exposure-response analyses
- **Immunogenicity** of all drugs, measured by antidrug antibody and neutralizing antibody assays
- **Patient-reported outcomes:** change from baseline in NCCN/FACT FBISI-18 DRS-P score

Exploratory endpoints

- Disease and health-related QOL (NCCN/FACT FBISI-18 subscales, and EQ-5D-5L index score and VAS)
- Biomarker analyses

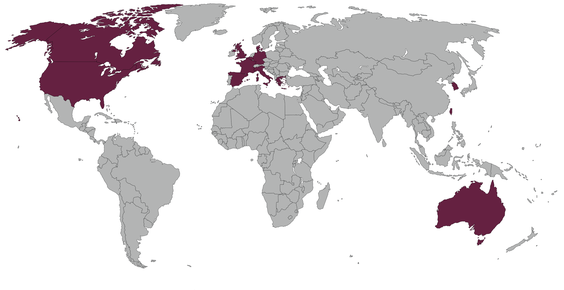
AE, adverse event; **DRS-P**, Disease-Related Symptoms–Physical; **EQ-5D-5L**, EuroQol 5 dimensions questionnaire; **NCCN/FACT FBISI-18**, NCCN/FACT Bladder Symptom Index-18; **OS**, overall survival; **PFS**, progression-free survival; **PK**, pharmacokinetics; **QOL**, quality of life; **VAS**, visual analog scale.

STATISTICAL ANALYSES

- Data in the avelumab monotherapy group is planned to be extended by combining with data from an external source, ie, the JAVELIN Bladder 100 trial[14]
- Survival analyses will be evaluated using HRs with CIs estimated by the Cox proportional hazards model; median PFS and corresponding 2-sided 95% CIs will be calculated according to Brookmeyer and Crowley
- Electronic patient-reported outcome (ePRO) assessments will be conducted every 2 weeks, in line with avelumab infusions, until the occurrence of progressive disease; if the patient continues treatment, ePROs will be conducted every 4 weeks

ENROLLMENT STATUS

Study enrollment for JAVELIN Bladder Medley is currently ongoing, expanding to ≈100 sites in Asia, Australia, Europe, and North America



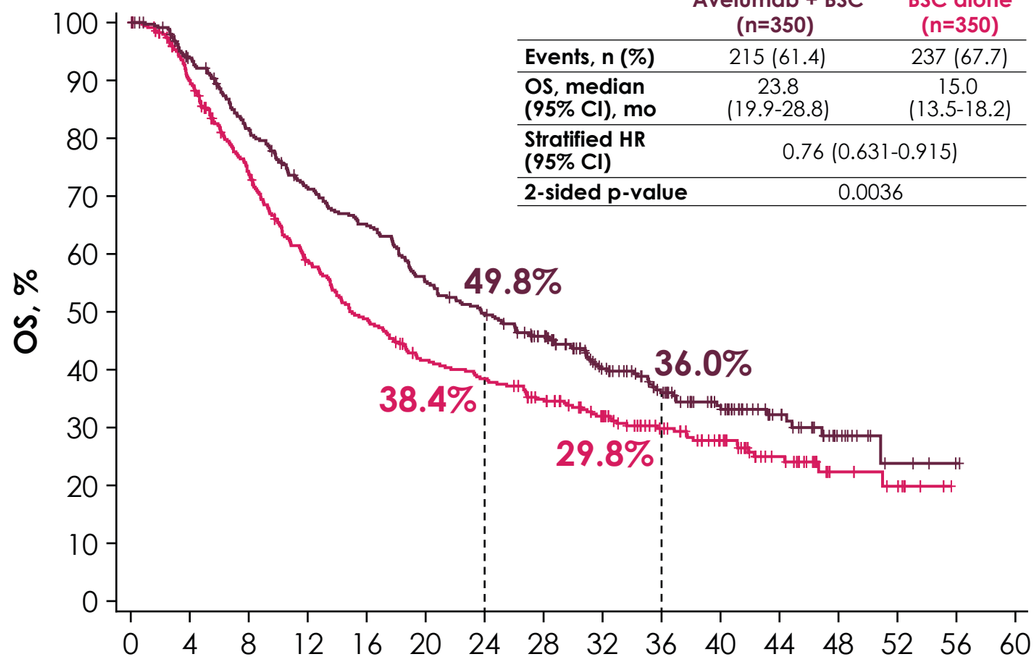
REFERENCES 1. NCCN Clinical Practice Guidelines: Bladder Cancer. V2.2022. **2.** Sung H, et al. CA Cancer J Clin. 2021;71:209-49. **3.** Powles T, et al. J Clin Oncol. 2022;40(Suppl 6). Abstract 487. **4.** Powles T, et al. Ann Oncol. 2022;33(3):244-58. **5.** Cathomas R, et al. Eur Urol. 2022;81:95-103. **6.** Bardia A, et al. N Engl J Med. 2021;384(15):1529-41. **7.** Goldenberg DM, et al. Oncotarget. 2015;6:22496-512. **8.** Goldenberg DM, et al. MAbs. 2019;11(6):987-95. **9.** Xu C, et al. J Immunother Cancer. 2021;9(Suppl 2). Abstract A351. **10.** Miyazaki T, et al. J Immunother Cancer. 2020;9(5):e002024. **11.** Heery CR, et al. Lancet Oncol. 2017;18(5):587-98. **12.** Boyerinas B, et al. Cancer Immunol Res. 2015;3(10):1148-57. **13.** Powles T, et al. Nat Med. 2021;27:2200–11. **14.** Powles T, et al. N Engl J Med. 2020;383(13):1218-30.

DISCLOSURES J. Hoffman-Censits has served in consulting or advisory roles for Seagen and reports other disclosures for Ikena Oncology, QED Therapeutics, and Seagen. **P. Grivas** has served in consulting or advisory roles for 4D Pharma PLC, AstraZeneca, Astellas Pharma, BostonGene, Bristol Myers Squibb, Dynavia Health, Exelixis, Fresenius Kabi, G1 Therapeutics, Genentech/Roche, Gilead Sciences, GlaxoSmithKline, Guardant Health, Infinity Pharmaceuticals, Janssen, Lucence Health, Merck & Co., Kenilworth, NJ, Mirati Therapeutics, Pfizer, PureTech, QED Therapeutics, Regeneron Pharmaceuticals, Seagen, Silverback Therapeutics, 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, G1 Therapeutics, Gilead Sciences, GlaxoSmithKline, Merck & Co., Kenilworth, NJ, Mirati Therapeutics, Pfizer, QED Therapeutics, and the healthcare business of Merck KGaA, Darmstadt, Germany. **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, Seagen, 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 research funding from Astellas Pharma, AstraZeneca, Bristol Myers Squibb, Eisai, Exelixis, Ipsen, Johnson & Johnson, Merck & Co., Kenilworth, NJ, Novartis, Pfizer, Roche, Seagen, and the healthcare business of Merck KGaA, Darmstadt, Germany. **D. Martincic** has served in consulting or advisory roles for AstraZeneca, Bristol Myers Squib, and the healthcare business of Merck KGaA, Darmstadt, Germany; and reports speakers services for AstraZeneca, Bristol Myers Squib, Daichi Sankyo, Regeneron, Sanofi, and the healthcare business of Merck KGaA, Darmstadt, Germany. **J. Hawley** has served in consulting or advisory roles for Seagen and has received institutional research funding from AstraZeneca, Bristol Myers Squibb, Dendreon, and Regeneron. **K. Tyroller** and **K. Tadjalli Mehr** report employment by the healthcare business of Merck KGaA, Darmstadt, Germany, and stock and other ownership interests in Merck KGaA, Darmstadt, Germany. **S. Seeberger, S. Guenther**, and **N. Jacob** report employment by the healthcare business of Merck KGaA, Darmstadt, Germany. **N. Hahn** has received institutional research funding from Astex, AstraZeneca, Bristol Myers Squibb, Genentech, HTG Molecular Diagnostics, Incyte, Inovio, Merck & Co., Kenilworth, NJ, Pieris, and Seagen; has served in consulting or advisory roles for BioGears, Boehringer Ingelheim, Champions Oncology, CicloMed, Ferring, Genentech, GlaxoSmithKline, Guidepoint Global, Health Advances, Incyte, Janssen, KeyQuest Health, Mirati Therapeutics, Merck & Co., Kenilworth, NJ, Pfizer, Protara Therapeutics, ReMeGen, Seagen, the healthcare business of Merck KGaA, Darmstadt, Germany, TransMed, and Verity Pharmaceuticals; and has received honoraria from the Bladder Cancer Academy, Creative Educational Concepts, and the Large Urology Group Practice Association. **ACKNOWLEDGMENTS** This trial is sponsored by the healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945) as part of an alliance between the healthcare business of Merck KGaA, Darmstadt, Germany and Pfizer. Medical writing support was provided by Sophie Saunders of Clinical Thinking and was funded by the healthcare business of Merck KGaA, Darmstadt, Germany and Pfizer.

Abstract No. 665. Presented at the Society for Immunotherapy of Cancer's (SITC) 37th Annual Meeting & Pre-Conference Programs (SITC 2022), November 8-12, 2022; Boston, MA, USA.

OS and investigator-assessed PFS from the JAVELIN Bladder 100 trial

OS

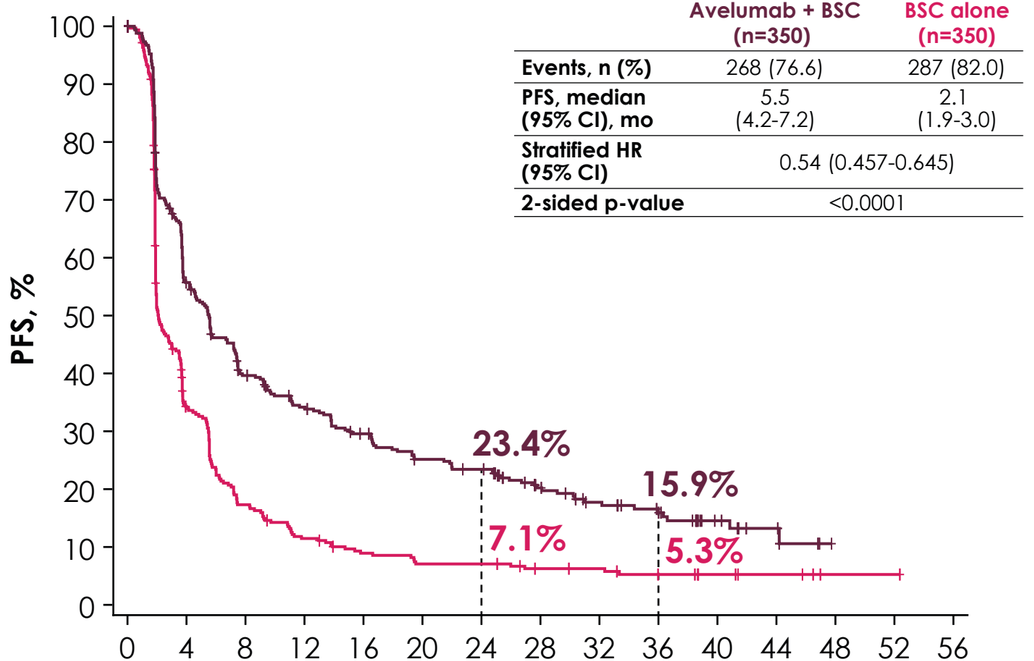


	Avelumab + BSC (n=350)	BSC alone (n=350)
Events, n (%)	215 (61.4)	237 (67.7)
OS, median (95% CI), mo	23.8 (19.9-28.8)	15.0 (13.5-18.2)
Stratified HR (95% CI)	0.76 (0.631-0.915)	
2-sided p-value	0.0036	

No. at risk

Avelumab + BSC	350	318	274	237	216	183	164	140	99	74	53	31	13	4	1	0	
BSC	350	304	243	190	158	131	121	103	82	62	46	27	10	7	0		

PFS



	Avelumab + BSC (n=350)	BSC alone (n=350)
Events, n (%)	268 (76.6)	287 (82.0)
PFS, median (95% CI), mo	5.5 (4.2-7.2)	2.1 (1.9-3.0)
Stratified HR (95% CI)	0.54 (0.457-0.645)	
2-sided p-value	<0.0001	

No. at risk

Avelumab + BSC	350	182	126	105	88	73	67	43	32	25	12	6	0				
BSC	350	101	51	33	24	19	19	14	13	9	6	4	1	1	0		

BSC, best supportive care; **HR**, hazard ratio; **OS**, overall survival; **PFS**, progression-free survival.

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

Avelumab combined with other anticancer drugs as first-line maintenance treatment in people with advanced urothelial cancer: JAVELIN Bladder Medley study design

JAVELIN

View scientific abstract

The full title of this abstract is: JAVELIN Bladder Medley: a phase 2 trial of avelumab in combination with other antitumor drugs as first-line maintenance therapy for advanced urothelial carcinoma

Please note this summary only contains information from the scientific abstract

View scientific abstract

Date of summary: November 2022

For more information on this study, go to: https://clinicaltrials.gov/ct2/show/NCT05327530

Pronunciations

Medical terms pronunciations

Avelumab <a-VEL-yoo-mab> **Urothelial** <YOOR-oh-THEE-lee-ul>

Sacituzumab govitecan <SAK-ih-TOO-zoo-mab GOH-vih-TEE-kan>

Key takeaways

What are the key takeaways from this summary?

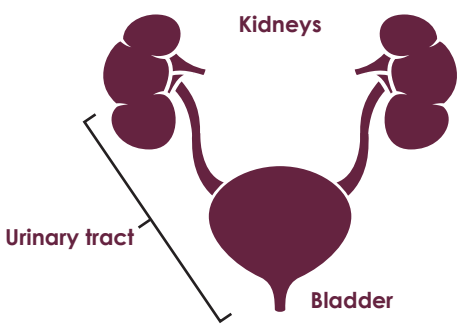
- In the previously reported JAVELIN Bladder 100 study, avelumab first-line maintenance treatment, which is given after first-line chemotherapy, helped people with advanced urothelial cancer live longer than people who were not treated with avelumab
  - A plain language summary of the overall results from the JAVELIN Bladder 100 study is available **by clicking here**
- In the JAVELIN Bladder Medley study, researchers want to find out how well avelumab first-line maintenance treatment works when it is combined with other anticancer drugs to treat people with advanced urothelial cancer. Researchers will also look at the side effects people have when they receive avelumab combined with other anticancer drugs
- The results from this study will show if the benefit of avelumab first-line maintenance treatment can be improved by combining avelumab with other anticancer drugs for people with advanced urothelial cancer
- The study is ongoing, and results are not available yet

Background

What will 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 and into nearby tissues (also known as locally advanced) or to other organs (also known as metastatic)



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 urothelial cancer stops growing or shrinks after first-line chemotherapy, they may then receive avelumab, a different treatment. This is called maintenance treatment. It aims to maintain the benefit of first-line chemotherapy and 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 **by clicking here**

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 are sacituzumab govitecan, M6223, and NKTR-255?

- Sacituzumab govitecan, M6223, and NKTR-255 are three different anticancer drugs
- Sacituzumab govitecan attaches to a protein that is found in high levels on some urothelial cancer cells and may help to destroy them. It is approved to treat people with advanced urothelial cancer that has gotten worse after previous treatment with chemotherapy and immunotherapy
- M6223 and NKTR-255 attach to different proteins on immune cells. They can also help the body's immune system find and destroy cancer cells
- These three drugs work in ways that when combined with avelumab may help people live longer than avelumab alone

What is the JAVELIN Bladder Medley study?

- The JAVELIN Bladder Medley study is looking at avelumab in combination with other anticancer drugs as first-line maintenance treatment for people with advanced urothelial cancer
- All the people taking part in the study will have received first-line chemotherapy and their cancer will have disappeared, shrunk, or stopped growing. They will be put into four treatment groups
- People will receive treatment until any of the following things happen:
  - Their cancer starts growing again and they can no longer do daily activities
  - They have severe side effects (meaning side effects that limit daily activities such as bathing and dressing, require hospital care, cause lasting problems, or are life threatening)
  - They do not want to take part in the study any more
  - They start receiving another new anticancer treatment

What do the researchers want to find out?

Researchers want to see if combining avelumab with other anticancer drugs as first-line maintenance treatment will help people with advanced urothelial cancer live longer without their cancer getting worse. They also want to see the side effects of these combination treatments

Study design

What will happen during the study?

Who will take part in the study?

People aged 18 or older with advanced urothelial cancer who received first-line chemotherapy

252 people whose cancer did not get worse with first-line chemotherapy

- **36** people will receive only avelumab
- **72** people will receive avelumab + sacituzumab govitecan
- **72** people will receive avelumab + M6223
- **72** people will receive avelumab + NKTR-255

- People from Asia, Australia, Europe, and North America are being included in this study
- The study began in June 2022

Aims of this study

What will the researchers look at?

- Researchers will look at the following in all treatment groups:
  - How long people live without their cancer getting worse
  - How many people have side effects
  - How long people live overall

Conclusions

What will be the main conclusions reported by the researchers?

- The results from the JAVELIN Bladder Medley study will show how well avelumab works when combined with other anticancer drugs as first-line maintenance treatment for people with advanced urothelial cancer
  - The study will also show how safe these combination treatments are
- The study results will help determine if the known benefit of avelumab first-line maintenance treatment can be improved by combining it with other anticancer drugs
- The JAVELIN Bladder Medley study is ongoing, and results will be reported in the future

Disclaimers

Avelumab is approved to treat the condition that is discussed in this summary. Avelumab is not approved for the investigational use in the combination treatment groups (ie, groups 2, 3, and 4). Its safety and efficacy in these uses have not been established. Sacituzumab govitecan is not approved for this investigational use; its safety and efficacy in this use have not been established. M6223 and NKTR-255 are investigational compounds; their safety and efficacy have not been established. The study described is ongoing. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study.

Study sponsors

Who is sponsoring this study?

the healthcare business of Merck KGaA, Darmstadt, Germany
Frankfurter Strasse 250
Darmstadt, 64293, Germany
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:
SITC 2022 Scientific Abstract
https://clinicaltrials.gov/ct2/show/NCT05327530

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

Writing support for this summary was provided by Sophie Saunders of Clinical Thinking and was funded by the healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945) and Pfizer.