

Lung, Kidney and Neuroendocrine Tumor Cancer Studies Led by Dana-Farber Presented at ESMO Congress

Other studies focused on bladder cancer, prostate cancer and liquid biopsies.

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Novel treatments, combination therapies, and personalized medicine headline several studies led by [Dana-Farber Cancer Institute](#) and presented for the first time at the [European Society of Medical Oncology \(ESMO\) Congress 2023](#) in Madrid, Spain. The studies will be presented both in-person and online on October 20-24, 2023. A full list of Dana-Farber oral abstracts is available [here](#).

A pivotal lung cancer study (LBA65) led by Pasi Jänne, MD, PhD, director of the Lowe Center for Thoracic Oncology, looking at the efficacy and safety of adagrasib [Krazati] with pembrolizumab [Keytruda] in patients who have advanced non-small-cell lung cancer (NSCLC) with a KRASG12C mutation will be presented as a late-breaking abstract in the Proffered Paper Session: NSCLC, metastatic, on Friday, October 20, 2023, 10:40am ET (16:40 CEST). Data from the Phase 2 KRYSTAL-7 trial will be presented.

Toni Choueiri, MD, director of the [Lank Center for Genitourinary Cancer](#), led a Phase 3 study (LBA88) looking at belzutifan [Welireg] versus everolimus [Afinitor and generic equivalents] in patients with previously treated advanced clear cell renal cell carcinoma (ccRCC). Choueiri is the senior author on the LITESPARK-005 study and data from the randomized open-label trial will be presented for the first time in the Proffered Paper Session 2: Genitourinary tumors, non-prostate, on Saturday, October 21, 2023, 8:55am ET (14:55 CEST). Choueiri will also present data from the phase 2 LITESPARK-003 study (LBA87) which looks at belzutifan in combination with cabozantinib for advanced ccRCC during the same session at 8:45am ET (14:45 CEST).

Data from the Phase 3 CABINET study (LBA53) in advanced neuroendocrine tumors (NET) will be presented for the first time by Jennifer Chan, MD, MPH, clinical director of the Gastrointestinal Cancer Center. The double-blinded study looks at cabozantinib [Cometriq or Cabometyx] versus placebo for advanced NET after progression on prior therapy. Chan will present the findings in a Proffered Paper Session: NETs and endocrine tumors, on Sunday, October 22, 2023, at 2:40am ET (8:40 CEST).

Other key research from Dana-Farber shows new treatments and advances in personalized medicine in prostate, head and neck, bladder, and many other cancer types. Select studies include:

Combination of two antibody-drug conjugates found safe in patients with advanced bladder cancer, may have implications in other cancer types

In patients with metastatic urothelial carcinoma (mUC) who progressed on prior treatments, the combination of antibody-drug conjugates (ADC) sacituzumab govitecan [Trodely] plus enfortumab vedotin [Padcev] was found safe with encouraging efficacy. Data from the Phase 1 double antibody-drug conjugate trial, dubbed the DAD trial, shows the combination of these unique ADCs, which have different payloads with different targets, did not present any new toxicity signals. Furthermore, the data shows robust clinical activity in this small trial with an objective response rate of 70%. To the researchers' knowledge, this is the first study to combine two ADCs in any malignancy and they plan to study this combination further in a Phase 2 expansion. The data presented at ESMO on double antibody-drug conjugates may have implications beyond bladder cancer in other malignancies.

Bradley McGregor, MD, the director of Clinical Research at the Lank Center for Genitourinary Cancer, first author, will present findings from the phase 1 DAD trial during the Proffered Paper Session 1: Genitourinary tumors, non-prostate (abstract 23600) during ESMO on October 21, 2023, 3:10am ET (9:10 CEST). Joaquim Bellmunt, MD, PhD, director of the Bladder Cancer Center, is senior author.

Largest epigenomic cell-free DNA dataset reported to date

Cancer cells shed DNA into the bloodstream, and analyzing this DNA can help doctors diagnose or monitor cancer using a blood sample in an approach known as a 'liquid biopsy.' Liquid biopsy has focused mainly on detecting changes in the DNA sequence (mutations) in cancer. In this study led by Dana-Farber, scientists developed a test that can measure changes in gene regulation – signals that turn genes on and off – from blood. This is the largest epigenomic cell-free DNA dataset reported to date. This approach may allow researchers to understand how cancer becomes resistant to treatment and to do a better job choosing the right treatment for a given patient.

Sylvan Baca, MD, PhD, a genitourinary oncologist at Dana-Farber, will present findings from: Clinical subtyping of cancer from blood based on comprehensive epigenomic profiling during the Proffered Paper Session 1: Basic science and translational research (abstract 12060) during ESMO on October 21, 2023, 4:25am ET (10:25 CEST). Dana-Farber's Toni Choueiri, MD, and Matthew Freedman, MD, are co-senior authors.

Prostate cancer study offers guidance on which patients most likely to benefit from treatment intensification

Radiation therapy and long-term androgen deprivation therapy (RT+ltADT) is standard of care treatment for patients with high-risk, locally advanced prostate cancer (HR/LA-PC). In this pooled

analysis of more than 3,500 patients with HR/LA-PC treated on randomized trials of RT+ltADT, researchers found outcomes vary significantly depending on the number of adverse risk factors and the presence of clinically node positive disease. The risk factors looked at were Gleason Score, T stage, PSA level, or node positive disease. Researchers found these risk factors highly prognostic. Poorer outcomes in overall survival and metastasis-free survival were seen in patients with two or three risk factors. The poorest outcomes were seen in patients with node-positive disease. Researchers say these findings have implications for selecting patients for intensification of therapy beyond RT+ltADT and will guide the interpretation of ongoing adjuvant trials in HR/LA-PC.

Praful Ravi, MB, BChir, MRCP, a genitourinary oncologist at Dana-Farber, will present findings from abstract 17700: Refining risk stratification in patients undergoing radiotherapy and long-term ADT for high-risk/locally advanced prostate cancer: an individual patient data analysis of randomized controlled trials from ICECaP consortium during the Proffered Paper Session: Genitourinary tumors, prostate during ESMO on October 20, 2023, 10:50am ET (16:50 CEST).

First targeted therapy found safe and shows anti-tumor activity in patients with rare head and neck cancer

HRAS mutations are seen in 4% to 8% of patients with recurrent and/or metastatic head and neck squamous cell carcinoma (HNSCC) and prognosis remains poor. Tipifarnib, a farnesyltransferase inhibitor that disrupts HRAS function, was found safe, tolerable and to have encouraging efficacy, according to the AIM-HN Phase 2 study. This study enrolled 59 patients who were treated with oral tipifarnib. Tipifarnib has previously shown promising activity in patients with HNSCC harboring high variant allele frequency (VAF). 50 of the 59 patients in this study had high VAF of $\geq 20\%$ (median 34%).

The primary endpoint was objective response rate (ORR). ORR was 30% by investigator assessment and 20% by independent review. Median progression free survival was 2.6 months and median overall survival 6.9 months. 44% of patients received immunotherapy prior to enrolling on the trial. Grade 3+ treatment-related adverse events (TRAEs) were observed in 56% of patients, however, only 7% discontinued treatment due to TRAEs. Ongoing combination studies are targeting adaptive resistance pathways (PI3K/mTOR/Akt) to further improve outcomes.

Dana-Farber's Robert Haddad, MD, the chief of the Division of Head and Neck Oncology, is senior author on the Phase 2 study evaluating tipifarnib in mHRAS in recurrent or metastatic head and neck squamous cell carcinoma (AIM-HN study). Findings will be presented during the Mini Oral Session: Head and neck cancer (abstract LBA47) during ESMO on October 21, 2023. 4:55am ET (10:55 CEST).

A full list of Dana-Farber oral presentations at the 2023 ESMO Congress is available [here](#).

This [news release](#) was published by Dana-Farber Cancer Institute on October 17, 2023.

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