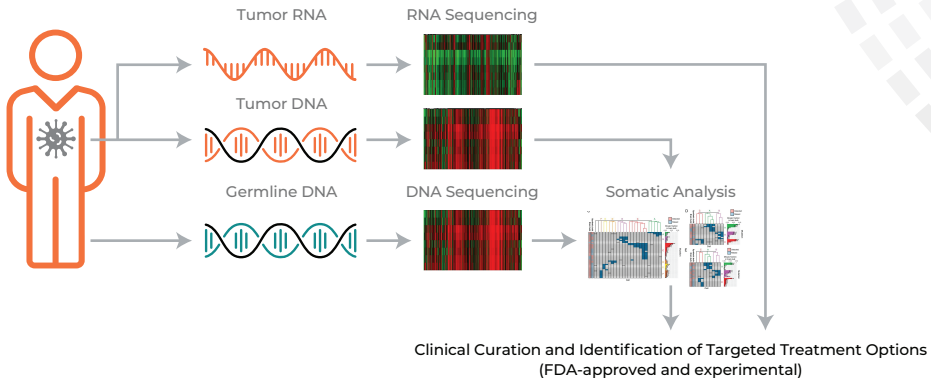
oncoExTra™ by EXACT SCIENCES

Covered by MEDICARE

Complete The Genomic Picture By Including DNA+RNA To Obtain The Most Actionable Insights For Therapy Selection

The OncoExTra™ test is an **ultra-comprehensive genomic profiling assay** that incorporates tumor whole-exome (DNA) and whole-transcriptome* (RNA) sequencing with paired tumor-normal analysis to identify alterations biomarkers in individuals diagnosed with advanced cancers. Findings are mapped to a knowledgebase of FDA-approved targeted treatment options as well as relevant clinical trial options.



WES (DNA) - Allows for comprehensive analysis of all protein-coding genes in a sample.

WTS (RNA) - Allows the identification of transcript variants and fusion genes that may be undetectable through conventional CGP tests which only employ DNA analysis.

Comprehensive Without Compromise

- The OncoExTra test interrogates ~20,000 genes.[3]
- IO signatures including tumor mutational burden (TMB) and microsatellite instability (MSI).
- 15 optional immunohistochemistry (IHC) stains† including PD-L1 (SP142, 22C3, SP263) and MMR (Mismatch Repair) proteins.
- Patient-matched tumor-normal sample to rule out benign variants.[3]

All About Actionability

- Reports clinically actionable mutations, copy number alterations, transcript variants/fusions through DNA and RNA analyses.
- FDA-approved therapies and clinical trial options based on the patient's results are also reported.
- In a clinical utilization study, at least one clinically actionable variant was identified in 83.9% of reports (1267/1509).[3]

*Whole-transcriptome sequencing with select variants reported in New York State
†IHC testing not currently available in New York State

According to one estimate, 20% of cancer morbidity occurs in tumors driven by translocations and gene fusions. Many of these alterations are actionable and may be missed by panel-based tests and WES alone.[1,2]

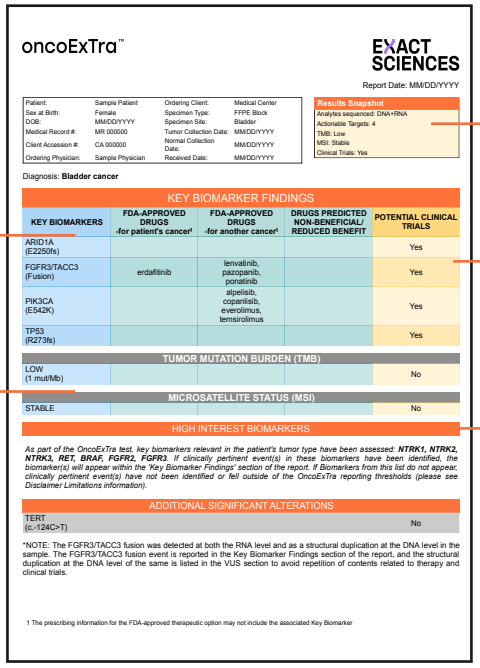
Case Study: Ultra-comprehensive genomic profiling uncovers rare fusion event in Bladder Cancer

- A **77 year-old-male** with a 35-pack year history presented to his primary care physician with a 2-month history of painless hematuria.
- Patient was referred to urology and cystoscopy **demonstrated a 4cm fungating mass** of the left posterior wall of the bladder.
- Biopsy of the mass confirmed urothelial carcinoma and palliative TURBT was scheduled to address the ongoing hematuria.
- Subsequent imaging studies demonstrated pulmonary lesions and **biopsy confirmed Stage IV Urothelial Carcinoma.**
- **Comprehensive genomic profiling with the OncoExTra test** was done on the lung biopsy specimen **where an FGFR3/TACC3 fusion** was found.
- The patient was deemed cisplatin eligible and treated with combination chemotherapy.
- Repeat imaging after 2 cycles of therapy **noted progressive disease** with an increase in the size and number of pulmonary nodules as well as a recurrence of hematuria.
- The patient was subsequently **treated with a tyrosine kinase Inhibitor** consistent with fusion findings after urologic intervention to address hematuria. After 3 months of treatment, a **partial response was noted on imaging** with no recurrence of the hematuria.

This case study is for educational purposes only and is not clinical, diagnostic, or treatment advice for any particular patient. Results and outcomes may vary. Providers should use their clinical judgment and experience when deciding how to diagnose or treat patients. Exact Sciences does not recommend or endorse any particular course of treatment or medical choice.

Targetable mutations and associated therapies

TMB & MSI Status



oncoExTra™

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Report Date: MM/DD/YYYY

Patient:	Sample Patient	Ordering Client:	Medical Center
Sex at Birth:	Female	Specimen Type:	FFPE Block
DOB:	MM/DD/YYYY	Specimen Site:	Bladder
Medical Record #:	MR 000000	Tumor Collection Date:	MM/DD/YYYY
Client Accession #:	CA 000000	Normal Collection Date:	MM/DD/YYYY
Ordering Physician:	Sample Physician	Received Date:	MM/DD/YYYY

Results Snapshot
Analytes sequenced: DNA+RNA
Actionable Targets: 4
TMB: Low
MSI: Stable
Clinical Trials: Yes

Diagnosis: **Bladder cancer**

KEY BIOMARKER FINDINGS

KEY BIOMARKERS	FDA-APPROVED DRUGS -for patient's cancer[1]	FDA-APPROVED DRUGS -for another cancer[1]	DRUGS PREDICTED NON-BENEFICIAL/ REDUCED BENEFIT	POTENTIAL CLINICAL TRIALS
ARID1A (E2250fs)				Yes
FGFR3/TACC3 (Fusion)	erdafitinib	lenvatinib, pazopanib, ponatinib		Yes
PIK3CA (E542K)		alpelisib, copanlisib, everolimus, temsirolimus		Yes
TP53 (R273fs)				Yes

TUMOR MUTATION BURDEN (TMB)

LOW (1 mut/Mb)	No

MICROSATELLITE STATUS (MSI)

STABLE	No

HIGH INTEREST BIOMARKERS

As part of the OncoExTra test, key biomarkers relevant in the patient's tumor type have been assessed: ***NTRK1, NTRK2, NTRK3, RET, BRAF, FGFR2, FGFR3****. If clinically pertinent event(s) in these biomarkers have been identified, the biomarker(s) will appear within the 'Key Biomarker Findings' section of the report. If Biomarkers from this list do not appear, clinically pertinent event(s) have not been identified or fell outside of the OncoExTra reporting thresholds (please see Disclaimer Limitations information).*

ADDITIONAL SIGNIFICANT ALTERATIONS

TERT (c.-124C>T)	No

*NOTE: The FGFR3/TACC3 fusion was detected at both the RNA level and as a structural duplication at the DNA level in the sample. The FGFR3/TACC3 fusion event is reported in the Key Biomarker Findings section of the report, and the structural duplication at the DNA level of the same is listed in the VUS section to avoid repetition of contents related to therapy and clinical trials.

1 The prescribing information for the FDA-approved therapeutic option may not include the associated Key Biomarker

Snapshot of Key Findings

Clinical Trial Options

High Interest Biomarkers

To Learn More: OncoExTra.com | To Order: OncoExTra.com/order

References: 1. Drenner, Basu GD, Goodman LJ, et al. The value of comprehensive genomic sequencing to maximize the identification of clinically actionable alterations in advanced cancer patients: a case series. Oncotarget. 2021; 12:1836-1847. **2.** Nikanjam M, Okamura R, Barkauskas DA, Kurzrock R. Targeting fusions for improved outcomes in oncology treatment. Cancer. 2020; 126:1315-1321. **3.** White T, Szelinger S, LoBello J, et al. Analytic validation and clinical utilization of the comprehensive genomic profiling test, Oncotarget 2021;12: 726-739

Disclaimer: The OncoExTra test is not a FDA cleared or approved IVD device or companion diagnostic for the referenced biomarkers and FDA approved therapies.

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OncoExTra has been validated according to the guidelines set forth by the New York State Department of Health. Whole exome (DNA) events have been validated to include point mutations, indels, and copy number alterations, as well as MSI analysis and TMB calculation. Whole transcriptome (RNA) has been validated to report on select fusion genes and special transcripts.