Donald Gleason Conference on Genitourinary Malignancies

Friday October 15th, 2021

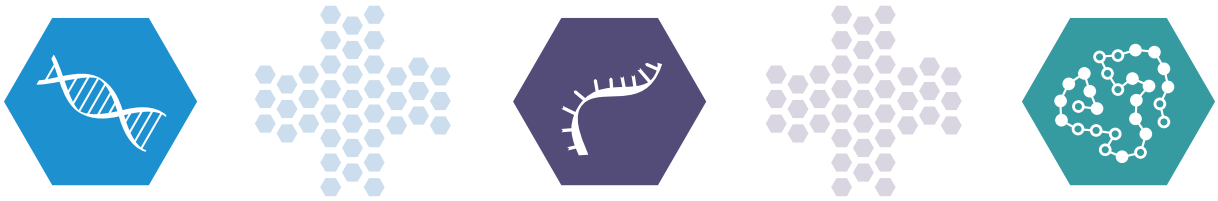
Online Exhibitor Portfolio

Thank you to our Exhibitors:

- Caris Life Sciences
- Decipher Urologic Cancers
- Janssen Biotech
- Myovant Sciences
- Seagen, Inc.

Comprehensive Tumor Profiling

The Caris comprehensive molecular profiling approach to assess DNA, RNA and proteins reveals a molecular blueprint to guide more precise and individualized treatment decisions from among 60+ FDA-approved therapies.



DNA

Whole Exome Sequencing
(Mutations, Indels & Copy Number Alterations)

RNA

Whole Transcriptome Sequencing
(Fusions & Variant Transcripts)

Protein

Immunohistochemistry

Technical Specifications

Sufficient tumor content (>20% tumor nuclei) must be present to complete all analysis. If you have any questions, please contact Customer Support at (888) 979-8669.

Technical Information	IHC	CISH	FISH
Sample Requirements *(see requsition for full details)*	1 unstained slide at 4µm thickness from FFPE block, with evaluable tumor present, per IHC test	1 unstained slide at 4µm thickness from FFPE block, with at least 100 evaluable tumor cells present, per CISH test	2 unstained slides at 4µm thickness from FFPE block, with at least 100 evaluable cells present and 10% tumor, per FISH test
Sensitivity/Specificity	>95%	>95%	>95%

Technical Information	NGS (Whole Exome - DNA)	NGS (Whole Transcriptome - RNA)
Sample Requirements	FFPE block or 10 unstained slides with a minimum of 20% malignant origin for DNA and 10% malignant origin for RNA. Needle biopsy is also acceptable (4-6 cores).	
Tumor Enrichment (when necessary)	Microdissection to isolate and increase the number of cancer cells to improve test performance and increase the chance for successful testing from small tumor samples	
Number of Genes	~22,000 genes	
Average Depth of Coverage (DNA) Average Read Count (RNA)	1,000x for 720+ clinical and research genes and 400-500x for all other genes	60 million
Positive Percent Agreement (PPA)	> 95% for base substitutions at ≥ 5% mutant allele frequency; > 99% for indels at ≥ 5% mutant allele frequency; >95% for copy number alterations (amplifications ≥ 6 copies)	>97%
Negative Percent Agreement (NPA)	>99%	>99%
Genomic and Transcriptomic Signatures and Panels	Microsatellite Instability (MSI) Tumor Mutational Burden (TMB) Loss of Heterozygosity (LOH) Caris FOLFIRSTai™* – AI predictor of FOLFOX response in metastatic colorectal adenocarcinoma	Human Leukocyte Antigen (HLA) Genotype*
	Caris GPSai™* Genomic Prevalence Score – CUP, atypical presentation or clinical ambiguity cases	

Caris Molecular Profiling Associations List

The list below details the biomarkers assessed, technology platforms utilized and associated therapies or clinical trials. **Biomarkers and therapy associations may vary by the tumor type submitted.** *Individual assay results are always included with the final report.*

Biomarker	Technology/Alteration	Agent
ALK	IHC, RNA Fusion	crizotinib, ceritinib, alectinib, brigatinib (NSCLC only), lorlatinib (NSCLC only)
	DNA Mutation	resistance to crizotinib, alectinib
AR	IHC	bicalutamide, leuprolide (salivary gland tumors only)
		enzalutamide, bicalutamide (TNBC only)
BRAF	DNA Mutation	vemurafenib, dabrafenib, cobimetinib, trametinib
		encorafenib + binimetinib (melanoma only)
		dabrafenib+trametinib (anaplastic thyroid and NSCLC only)
		atezolizumab + cobimetinib + vemurafenib (melanoma only)
		cetuximab + encorafenib (CRC only)
BRCA1/2	DNA Mutation	carboplatin, cisplatin, oxaliplatin
		niraparib (ovarian, prostate), olaparib (breast, cholangiocarcinoma, ovarian, pancreatic, prostate), rucaparib (ovarian, pancreatic, prostate), talazoparib (breast only), veliparib combination (pancreatic only)
		resistance to olaparib, niraparib, rucaparib with reversion mutation
EGFR	DNA Mutation	afatinib (NSCLC only)
		afatinib + cetuximab (T790M; NSCLC only)
		amivantamab (Exon 20 insertion; NSCLC only)
		erlotinib, gefitinib (NSCLC and CUP only)
		osimertinib, dacomitinib (NSCLC only)
ER	IHC	endocrine therapies
		everolimus (breast only)
		palbociclib, ribociclib, abemaciclib (breast only)
ERBB2 (HER2)	IHC, CISH, DNA Mutation, CNA	trastuzumab, lapatinib, neratinib (breast only), pertuzumab, T-DM1, fam-trastuzumab deruxtecan-nxki, tucatinib, margetuximab
	DNA Mutation	T-DM1 (NSCLC only)
ER/PR/ERBB2 (HER2)	IHC, CISH	sacituzumab govitecan (TNBC only)
ESR1	DNA Mutation	exemestane + everolimus, fulvestrant, palbociclib combination therapy (breast only)
		resistance to aromatase inhibitors (breast only)
FGFR2/3	DNA Mutation, RNA Fusion	erdafitinib (urothelial bladder only), pemigatinib, infigratinib (biliary tract cancers only)
HRR	DNA Mutation	olaparib (prostate only)
IDH1	DNA Mutation	temozolomide (high grade glioma only)
		ivosidenib (biliary tract cancers only)
KIT	DNA Mutation	imatinib
		regorafenib, sunitinib (both GIST only)
KRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to erlotinib/gefitinib (NSCLC only)
		resistance to trastuzumab, lapatinib, pertuzumab (CRC only)
		sotorasib (G12C-mutated, NSCLC only)
MET	RNA Exon Skipping, DNA Exon Skipping, CNA	capmatinib, crizotinib, tepotinib (all NSCLC only)
MGMT	Pyrosequencing (Methylation)	temozolomide (high grade glioma only)
MMR Deficiency	IHC, DNA Mutation	pembrolizumab, dostarlimab (endomentrial only)
MSI		pembrolizumab, nivolumab (CRC, small bowel adenocarcinoma), nivolumab+ipilimumab (CRC, small bowel adenocarcinoma)
MMR Proficiency	IHC, DNA Mutation	pembrolizumab + lenvatinib (endometrial only)
MSS		
NRAS	DNA Mutation	resistance to cetuximab, panitumumab (CRC only)
		resistance to trastuzumab, lapatinib, pertuzumab (CRC only)
NTRK1/2/3	RNA Fusion	entrectinib, larotrectinib
	DNA Mutation	resistance to larotrectinib, entrectinib
PALB2	DNA Mutation	olaparib (pancreatic and prostate), veliparib combination (pancreatic only)
PDGFRA	DNA Mutation	imatinib, avapritinib (GIST only), sunitinib
PD-L1	IHC	pembrolizumab (22c3 TPS in NSCLC; 22c3 CPS in cervical, esophageal, GEJ/gastric, head & neck, urothelial and non-urothelial bladder, vulvar)
		atezolizumab (SP142 IC urothelial bladder cancer and SP142 IC & TC NSCLC)
		pembrolizumab + chemotherapy (22c3 CPS in TNBC only)
		atezolizumab + nab-paclitaxel (SP142 IC in TNBC only)
		nivolumab/ipilimumab combination (28-8 NSCLC only)
		cemiplimab (22c3 TPS NSCLC only)
PIK3CA	DNA Mutation	alpelisib + fulvestrant (breast only)
POLE	DNA Mutation	pembrolizumab (endometrial and CRC only)
PR	IHC	endocrine therapies
RET	RNA Fusion	cabozantinib, vandetanib, selpercatinib, pralsetinib (NSCLC only)
	DNA Mutation	vandetanib, cabozantinib, selpercatinib (thyroid only); resistance to vandetanib, cabozantinib
ROS1	IHC, RNA Fusion	crizotinib, ceritinib, entrectinib, lorlatinib (NSCLC only)
TMB	DNA Mutation	pembrolizumab

IHC: Immunohistochemistry **CISH:** Chromogenic *in situ* Hybridization **CNA:** Copy Number Alteration (DNA)
HRR (Homologous Recombination Repair) genes: ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L
Note: in certain instances, some biomarkers included in MI Profile or genes ordered individually will not associate with commercially available cancer therapies or clinical trials.

Biomarker Analysis by Tumor Type

The information below details the biomarkers analyzed by technology for the tumor type submitted. Before ordering testing services, please refer to the profile menu online (www.CarisLifeSciences.com/profiling-menu) to view the most up-to-date listing of biomarkers that will be performed. Tests may vary if insufficient tumor samples are submitted.

MI Profile™						
Tumor Type	Immunohistochemistry (IHC)	Other	MI Tumor Seek™			
			Whole Exome Sequencing (WES)		Whole Transcriptome Sequencing (WTS)	
			DNA Alterations	Genomic Signatures	RNA Alterations	Genomic Signatures
Bladder	MMR, PD-L1 (SP142 and 22c3)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Breast	AR, ER, Her2/Neu, MMR, PD-L1 (SP142, 22c3), PR, PTEN		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Cancer of Unknown Primary – Female	AR, ER, Her2/Neu, MMR, PD-L1(SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Cancer of Unknown Primary – Male	AR, Her2/Neu, MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Cervical	ER, MMR, PD-L1 (22c3), PR		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Cholangiocarcinoma/ Hepatobiliary	Her2/Neu, MMR, PD-L1 (SP142)	Her2 *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Colorectal and Small Intestinal	Her2/Neu, MMR, PD-L1 (SP142), PTEN		Mutations, Indels, CNA	MSI, TMB, LOH, Caris FOLFIRSTai™ *(CRC only)*	Fusions, Variant Transcripts	HLA
Endometrial	ER, MMR, PD-L1 (SP142), PR, PTEN		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Esophageal Cancer	Her2/Neu, MMR, PD-L1 (22c3)	EBER *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Gastric/GEJ	Her2/Neu, MMR, PD-L1 (22c3)	EBER, Her2 *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
GIST	MMR, PD-L1 (SP142), PTEN		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Glioma	MMR, PD-L1 (SP142)	MGMT Methylation *(Pyrosequencing)*	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Head & Neck	MMR, p16, PD-L1 (22c3)	EBER, HPV *(Chromogenic in situ Hybridization)*, HPV reflex to confirm p16 result	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Kidney	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Lymphoma/Leukemia			Mutations, Indels, CNA	TMB	Fusions, Variant Transcripts	HLA
Melanoma	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Merkel Cell	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Neuroendocrine	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Non-Small Cell Lung	ALK, MMR, PD-L1 (22c3, 28-8 and SP142), PTEN		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Ovarian	ER, MMR, PD-L1 (22c3), PR		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Pancreatic	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Prostate	AR, MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Salivary Gland	AR, Her2/Neu, MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Sarcoma	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Small Cell Lung	MMR, PD-L1(22c3)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Thyroid	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Uterine Serous	ER, Her2/Neu, MMR, PD-L1 (SP142), PR, PTEN	Her2 *(Chromogenic in situ Hybridization)*	Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Vulvar Cancer (SCC)	ER, MMR, PD-L1 (22c3), PR		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA
Other Tumors	MMR, PD-L1 (SP142)		Mutations, Indels, CNA	MSI, TMB, LOH	Fusions, Variant Transcripts	HLA

Caris FOLFIRSTai™: AI predictor of FOLFOX response in metastatic colorectal adenocarcinoma. **MMR = Mismatch Repair proteins: MLH1, MSH2, MSH6, PMS2**

Next-Generation Sequencing Gene List

Whole Exome Sequencing – Genes most commonly associated with cancer below.

Point Mutations and Indels (DNA)

ABL1	BCOR	FANCF	HIST1H3B	LZTR1	NBN	PPP2R1A	RHOA	TMEM127
AIP	BTK	FANCI	HIST1H3C	MAPK1	NOTCH1	PPP2R2A	SDHA	VHL
AKT1	CD79B	FANCM	HNF1A	MAPK3	NRAS	PRKACA	SDHAF2	XRCC1
AMER1	CDH1	FAT1	HOXB13	MAX	NTHL1	PRKDC	SETD2	YES1
AR	CDK12	FOXL2	HRAS	MED12	PARP1	RABL3	SMARCA4	
ARAF	CXCR4	FYN	KDM5C	MPL	PHOX2B	RAD51B	SOCS1	
ATRX	DNMT3A	GLI2	KDM6A	MSH3	PIK3CB	RAD51C	SPOP	
B2M	EPHA2	GNA11	KDR	MST1R	PMS1	RAD51D	SRC	
BCL2	FANCB	HDAC	LYN	MUTYH	POLD1	RAD54L	TERT	

Point Mutations, Indels and Copy Number Alterations (DNA)

ALK	BRIP1	CSF1R	FANCC	FLT4	KIT	MRE11	PALB2	PTPN11	SMARCE1
APC	CARD11	CTNNA1	FANCD2	FUBP1	KMT2A	MSH2	PBRM1	RAD50	SMO
ARID1A	CBFB	CTNNB1	FANCE	GATA3	KMT2C	MSH6	PDGFRA	RAF1	SPEN
ARID2	CCND1	CYLD	FANCG	GNA13	KMT2D	MTOR	PDGFRB	RB1	STAT3
ASXL1	CCND2	DDR2	FANCL	GNAQ	KRAS	MYCN	PIK3CA	RET	STK11
ATM	CCND3	DICER1	FAS	GNAS	LCK	MYD88	PIK3R1	RNF43	SUFU
ATR	CDC73	EGFR	FBXW7	H3F3A	MAP2K1	NF1	PIM1	ROS1	TNFAIP3
BAP1	CDK4	EP300	FGFR1	H3F3B	MAP2K2	NF2	PMS2	RUNX1	TNFRSF14
BARD1	CDK6	ERBB2	FGFR2	IDH1	MAP2K4	NFE2L2	POLE	SDHB	TP53
BCL9	CDKN1B	ERBB3	FGFR3	IDH2	MAP3K1	NFKBIA	POT1	SDHC	TSC1
BLM	CDKN2A	ERBB4	FGFR4	IRF4	MEF2B	NPM1	PPARG	SDHD	TSC2
BMPR1A	CHEK1	ERCC2	FH	JAK1	MEN1	NSD1	PRDM1	SF3B1	U2AF1
BRAF	CHEK2	ESR1	FLCN	JAK2	MET	NTRK1	PRKAR1A	SMAD2	WRN
BRCA1	CIC	EZH2	FLT1	JAK3	MITF	NTRK2	PTCH1	SMAD4	WT1
BRCA2	CREBBP	FANCA	FLT3	KEAP1	MLH1	NTRK3	PTEN	SMARCB1	

Whole Exome Sequencing – Genomic Stability Testing (DNA)

Microsatellite Instability (MSI)	Tumor Mutational Burden (TMB)	Loss of Heterozygosity (LOH)

Whole Transcriptome Sequencing – Genes most commonly associated with cancer listed below.

Fusions (RNA)								Variant Transcripts (RNA)
ABL	BRD3	FGFR3	INSR	MYB	NUMBL	PRKCA	RSPO3	AR-V7
AKT3	BRD4	ERG	MAML2	NOTCH1	NUTM1	PRKCB	TERT	
ALK	EGFR	ESR1	MAST1	NOTCH2	PDGFRA	RAF1	TFE3	EGFR vIII
ARHGAP26	EWSR1	ETV1	MAST2	NRG1	PDGFRB	RELA	TFEB	
AXL	FGR	ETV4	MET	NTRK1	PIK3CA	RET	THADA	MET Exon 14 Skipping
BCR	FGFR1	ETV5	MSMB	NTRK2	PKN1	ROS1	TMPRSS2	
BRAF	FGFR2	ETV6	MUSK	NTRK3	PPARG	RSPO2		

Whole Transcriptome Sequencing – Genomic Stability Testing (RNA)

Human Leukocyte Antigen (HLA) Genotype

** Not available in New York State.*

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Intl: 00 41 21 533 53 00 | InternationalSupport@CarisLS.com

Where Molecular Science Meets Artificial Intelligence.

CARIS®

Sales Representative: Andrew Hanson Phone Number: 1 (763)-245-0620
Email: andrew.hanson@veracyte.com Webpage: https://decipherbio.com

Product Information:

Decipher Urologic Cancers, a wholly-owned subsidiary of Veracyte, Inc., is focused on genomic testing to help treatment planning for urologic cancers. The Decipher Prostate Genomic Classifier (Decipher Prostate) is a whole-transcriptome microarray that provides prostate cancer patients (post-biopsy and post-prostatectomy) with their genomic risk of metastasis as well as important prostate cancer-specific outcomes. It is comprised of 22 genes that span across seven biological pathways that are important in cancer pathophysiology.

Decipher genomic risk is derived solely from the genetic characteristics of the tumor, providing valuable information not available through already known clinical and pathological factors that is used to guide treatment decisions. The test has been validated in over 42 studies of more than 30,000 patients and is an accurate predictor of metastasis, prostate cancer-specific mortality, and overall survival.

- Decipher Prostate Biopsy helps determine which patients may be suitable candidates for active surveillance as well as those with more aggressive disease and may benefit from definitive therapy. For the patients who require treatment, the test can help decide the timing and intensity of the treatment.
- Decipher Prostate RP helps determine the timing and intensity (radiotherapy +/- hormone therapy) of treatment after radical prostatectomy.

Decipher is covered by Medicare for all patients with localized prostate cancer being considered for treatment. It is included in the National Comprehensive Cancer Network® (NCCN) Clinical Practice Guidelines for Prostate Cancer for use at diagnosis in the post-biopsy setting, as well as **uniquely recommended** in the post-prostatectomy setting for patients with adverse pathology and/or a persistent or rising PSA.

Following data published in a post-hoc analysis of Decipher in the practice-changing prospective randomized clinical trial, RTOG 96-01, the new guidelines (v1.2022) specifically state that men with high-risk Decipher scores (>0.6) after surgery with a rising PSA should be strongly considered for radiotherapy with concurrent hormone therapy.

Medicare Coverage & NCCN Guideline Approval Across Localized Prostate Cancer

		MEDICARE COVERAGE	NCCN GUIDELINES*
Decipher Prostate Biopsy	VERY LOW	✓	
	LOW	✓	✓
	FAVORABLE INTERMEDIATE	✓	✓
	UNFAVORABLE INTERMEDIATE	✓	✓
	HIGH	✓	✓
	VERY HIGH	✓	
	LYMPH NODE +	✓	
Decipher Prostate RP	UNDETECTABLE PSA	✓	✓
	PERSISTENT PSA	✓	✓
	RISING PSA	✓	✓

*Prostate Cancer NCCN Clinical Practice Guidelines v2.2021

NCCN Guidelines for Prostate Cancer *recommend* use of Decipher Prostate RP to individualize treatment discussions

Decipher Evidence-Based Treatment Considerations

POST-BIOPSY		
Clinical Decision	**Decipher Risk**	**May Consider**
Active Surveillance OR Definitive Therapy	Low	Active Surveillance [1-5]
	Intermediate / High	Definitive Therapy [1-5]
Radiation OR Radiation + ADT	Low	Radiation [1,4-6]
	Intermediate / High	Radiation + ADT [1,4-6]
Duration of Hormone Therapy with Radiation	Low	Radiation + Short-Term ADT [6]
	Intermediate / High	Radiation + Long-Term ADT [6]
Radical Prostatectomy	Low / Intermediate / High	Personalizing Treatment Planning [1]

RP = Radical Prostatectomy, RT = Radiotherapy, ADT = Androgen Deprivation Therapy

1. Vince Jr, RA et al. Prostate Cancer Prostatic Dis (2021).
2. Kim, HL et al. Prostate Cancer Prostatic Dis 22, 399-405 (2019).
3. Herlemann, A et al. Prostate Cancer Prostatic Dis 23, 136-143 (2020).
4. Berlin, A et al. Int J Radiat Oncol Biol Phys 103, 84-91 (2019).
5. Spratt, DE et al. J Clin Oncol 36, 581-590 (2018).
6. Nguyen, PL et al. Prostate Cancer Prostatic Dis 20, 186-192 (2017).
7. Den, RB et al. J Clin Oncol 33, 944-951 (2015).
8. Ross, AE et al. Prostate Cancer Prostatic Dis 19, 277-282 (2016).
9. Marascio, J et al. Prostate Cancer Prostatic Dis (2019).
10. Feng, FY et al. JAMA Oncol 7(4): 544-552 (2021).
11. Freedland, SJ et al. Eur Urol 70, 588-596 (2016).
12. Spratt, DE et al. Eur Urol 74, 107-114 (2018).

Decipher Evidence-Based Treatment Considerations

POST-RADICAL PROSTATECTOMY		
Clinical Decision	**Decipher Risk**	**May Consider**
PSA Monitoring OR Treatment	Low	PSA Monitoring [7-9]
	Intermediate	
	High	Treatment [7-9]
Radiation OR Radiation + ADT	Low	Radiation Alone [10-12]
	Intermediate	Radiation +/- ADT [10-12]
	High	Radiation + ADT [10-12]

RT = Radiotherapy, ADT = Androgen Deprivation Therapy

1. Vince Jr, RA et al. Prostate Cancer Prostatic Dis (2021).
2. Kim, HL et al. Prostate Cancer Prostatic Dis 22, 399-405 (2019).
3. Herlemann, A et al. Prostate Cancer Prostatic Dis 23, 136-143 (2020).
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12. Spratt, DE et al. Eur Urol 74, 107-114 (2018).

National Comprehensive Cancer Network (NCCN) Guidelines

The NCCN Clinical Practice Guidelines for Prostate Cancer v1.2022 ***recommend*** the use of Decipher Prostate:

Post-Biopsy Setting

- **PROS C:** Principles of Risk Stratification (Category 2A): "Patients with low or favorable intermediate-risk disease and life expectancy of ≥10 years may consider use of the following tumor-based molecular assays: **Decipher**…Patients with unfavorable intermediate- and high-risk disease and life expectancy of ≥10 years may consider the use of **Decipher**..."

Table 2. Tumor-Based Molecular Assays Can be Considered in Patients with Life Expectancy ≥10y as follows:						
	Very low risk	Low risk	Favorable intermediate risk	Unfavorable intermediate risk	High risk	Very high risk
Decipher	No	Yes	Yes	Yes	Yes	No

2022 NCCN Guidelines Recommend Decipher

National Comprehensive Cancer Network®

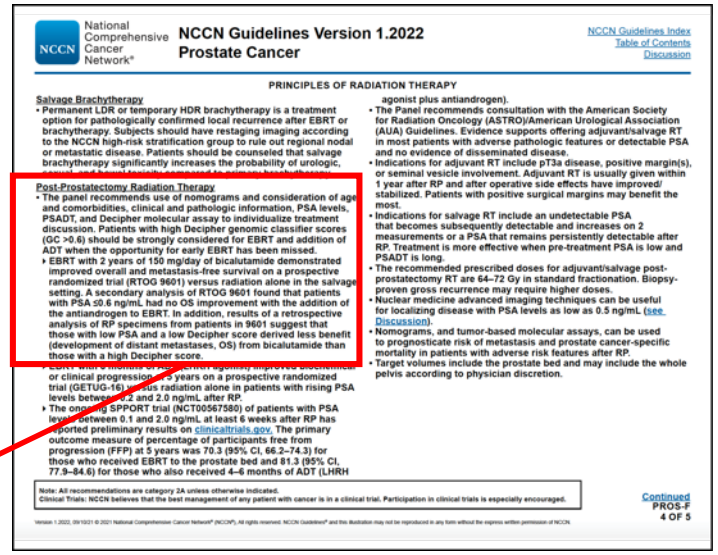
Post-Radical Prostatectomy Setting

- **Update based on results from a post-hoc analysis of Decipher in the NRG Oncology Phase 3 RCT RTOG 96-01**
  - **Decipher high-risk** men received strong benefit (in overall metastasis-free, and prostate cancer specific survival) from the addition of hormone therapy to radiotherapy, while **Decipher low-risk** patients received less benefit

Only genomic test *recommended* for use after radical prostatectomy

Post-Prostatectomy Radiation Therapy

- **The panel recommends use of nomograms and consideration of age and comorbidities, clinical and pathologic information, PSA levels, PSADT, and Decipher molecular assay to individualize treatment discussion. Patients with high Decipher genomic classifier scores (GC >0.6) should be strongly considered for EBRT and addition of ADT when the opportunity for early EBRT has been missed.**
  - **EBRT with 2 years of 150 mg/day of bicalutamide demonstrated improved overall and metastasis-free survival on a prospective randomized trial (RTOG 9601) versus radiation alone in the salvage setting. A secondary analysis of RTOG 9601 found that patients with PSA ≤0.6 ng/mL had no OS improvement with the addition of the antiandrogen to EBRT. In addition, results of a retrospective analysis of RP specimens from patients in 9601 suggest that those with low PSA and a low Decipher score derived less benefit (development of distant metastases, OS) from bicalutamide than those with a high Decipher score.**



NCCN Guidelines Version 1.2022
Prostate Cancer

PRINCIPLES OF RADIATION THERAPY

Salvage Brachytherapy

- Permanent LDR or temporary HDR brachytherapy is a treatment option for pathologically confirmed local recurrence after EBRT or brachytherapy. Subjects should have restaging imaging according to the NCCN high-risk stratification group to rule out regional nodal or metastatic disease. Patients should be counseled that salvage brachytherapy significantly increases the probability of urologic,

Post-Prostatectomy Radiation Therapy

- The panel recommends use of nomograms and consideration of age and comorbidities, clinical and pathologic information, PSA levels, PSADT, and Decipher molecular assay to individualize treatment discussion. Patients with high Decipher genomic classifier scores (GC >0.6) should be strongly considered for EBRT and addition of ADT when the opportunity for early EBRT has been missed.
  - EBRT with 2 years of 150 mg/day of bicalutamide demonstrated improved overall and metastasis-free survival on a prospective randomized trial (RTOG 9601) versus radiation alone in the salvage setting. A secondary analysis of RTOG 9601 found that patients with PSA ≤0.6 ng/mL had no OS improvement with the addition of the antiandrogen to EBRT. In addition, results of a retrospective analysis of RP specimens from patients in 9601 suggest that those with low PSA and a low Decipher score derived less benefit (development of distant metastases, OS) from bicalutamide than those with a high Decipher score.
- EBRT with a monthly prospective agonist improved disease-free or clinical progression at 5 years on a prospective randomized trial (GETUG-16) versus radiation alone in patients with rising PSA levels between 0.2 and 2.0 ng/mL after RP.
- The ongoing SPPORT trial (NCT00567580) of patients with PSA levels between 0.1 and 2.0 ng/mL at least 6 weeks after RP has reported preliminary results on clinicaltrials.gov. The primary outcome measure of percentage of participants free from progression (FFP) at 5 years was 70.3 (95% CI, 66.2–74.3) for those who received EBRT to the prostate bed and 81.3 (95% CI, 77.9–84.6) for those who also received 4–6 months of ADT (LHRH agonist plus antiandrogen).
- The Panel recommends consultation with the American Society for Radiation Oncology (ASTRO)/American Urological Association (AUA) Guidelines. Evidence supports offering adjuvant/salvage RT in most patients with adverse pathologic features or detectable PSA and no evidence of disseminated disease.
- Indications for adjuvant RT include pT3a disease, positive margin(s), or seminal vesicle involvement. Adjuvant RT is usually given within 1 year after RP and after operative side effects have improved/stabilized. Patients with positive surgical margins may benefit the most.
- Indications for salvage RT include an undetectable PSA that becomes subsequently detectable and increases on 2 measurements or a PSA that remains persistently detectable after RP. Treatment is more effective when pre-treatment PSA is low and PSADT is long.
- The recommended prescribed doses for adjuvant/salvage post-prostatectomy RT are 64–72 Gy in standard fractionation. Biopsy-proven gross recurrence may require higher doses.
- Nuclear medicine advanced imaging techniques can be useful for localizing disease with PSA levels as low as 0.5 ng/mL (see Discussion).
- Nomograms, and tumor-based molecular assays, can be used to prognosticate risk of metastasis and prostate cancer-specific mortality in patients with adverse risk features after RP.
- Target volumes include the prostate bed and may include the whole pelvis according to physician discretion.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Continued
PROS-F
4 OF 5

PROS-F: Post-Prostatectomy Radiation Therapy

Decipher Prostate recommendations are also described in PROS-8 (post-RP adverse features) & PROS-10 (post-RP persistent/ rising PSA)

European Association of Urology

Review – Prostate Cancer

A Systematic Review of the Evidence for the Decipher Genomic Classifier in Prostate Cancer

Neil K. Jairath[a,†], Alan Dal Pra[b,†], Randy Vince Jr.[c], Robert T. Dess[a], William C. Jackson[a], Jeffrey J. Tosoian[c], Sean M. McBride[d], Shuang G. Zhao[a], Alejandro Berlin[e], Brandon A. Mahal[b,f], Amar U. Kishan[g], Robert B. Den[h], Stephen J. Freedland[i,j], Simpa S. Salami[c], Samuel D. Kaffenberger[c], Alan Pollack[b], Phuoc Tran[k], Rohit Mehra[l], Todd M. Morgan[c], Adam B. Weiner[m], Osama Mohamad[n], Peter R. Carroll[o], Matthew R. Cooperberg[o], R. Jeffrey Karnes[p], Paul L. Nguyen[q], Jeff M. Michalski[r], Jonathan D. Tward[s], Felix Y. Feng[n], Edward M. Schaeffer[m], Daniel E. Spratt[a,]*

Setting	Indication	# Studies	# Patients
Biopsy	Active Surveillance	5	10,456
	Definitive Therapy	12	8,737
	Non-Metastatic Castrate Resistant	1	233
	Metastatic Hormone Sensitive	2	382
Post-RP	Early vs. Salvage Radiation	18	9,515
	Salvage Therapy Intensity	4	1,084
	TOTAL	**42**	**30,407**

An independent systematic review of **42 studies** and more than **30,000 patients** demonstrated that Decipher:

- is **independently prognostic** for overall survival, metastasis, PCSM, adverse pathology, and biochemical failure.
- is **more accurate** in stratifying patient risk than clinicopathologic variables alone.
- **impacts** treatment decisions and **improves** patient outcomes.

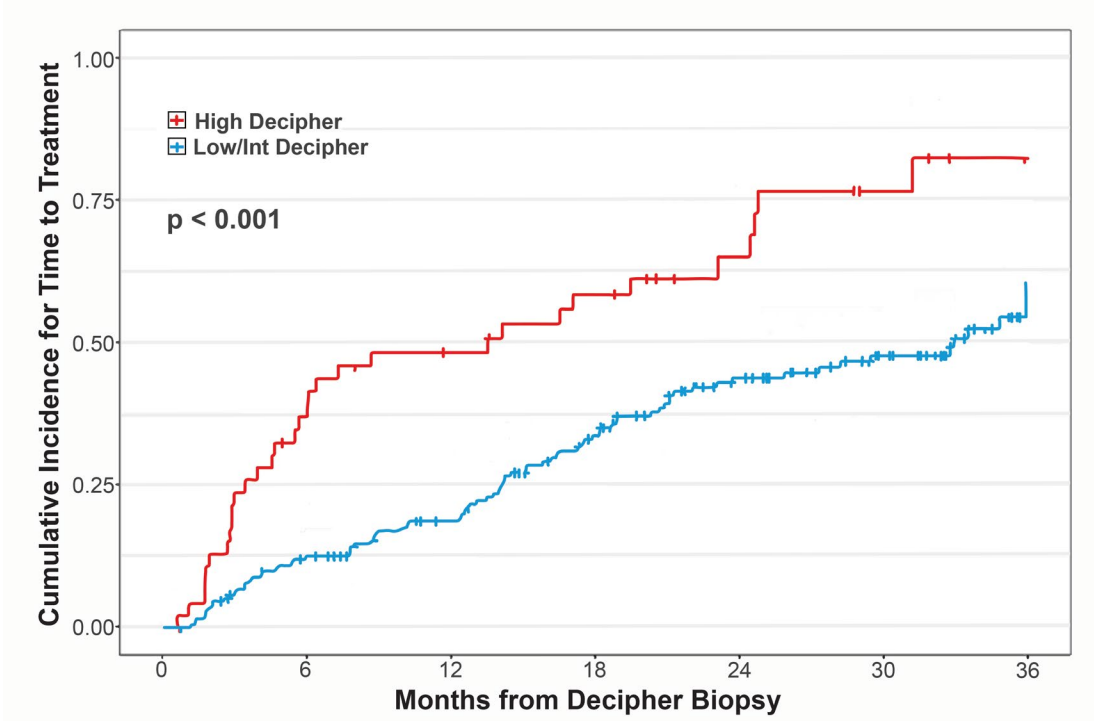
Jairath, NK *et al.* A Systematic Review of the Evidence for the Decipher Genomic Classifier in Prostate Cancer. *Eur Urol*, doi:10.1016/j.eururo.2020.11.021 (2021)

Prospective Registry Evidence for Decipher Biopsy

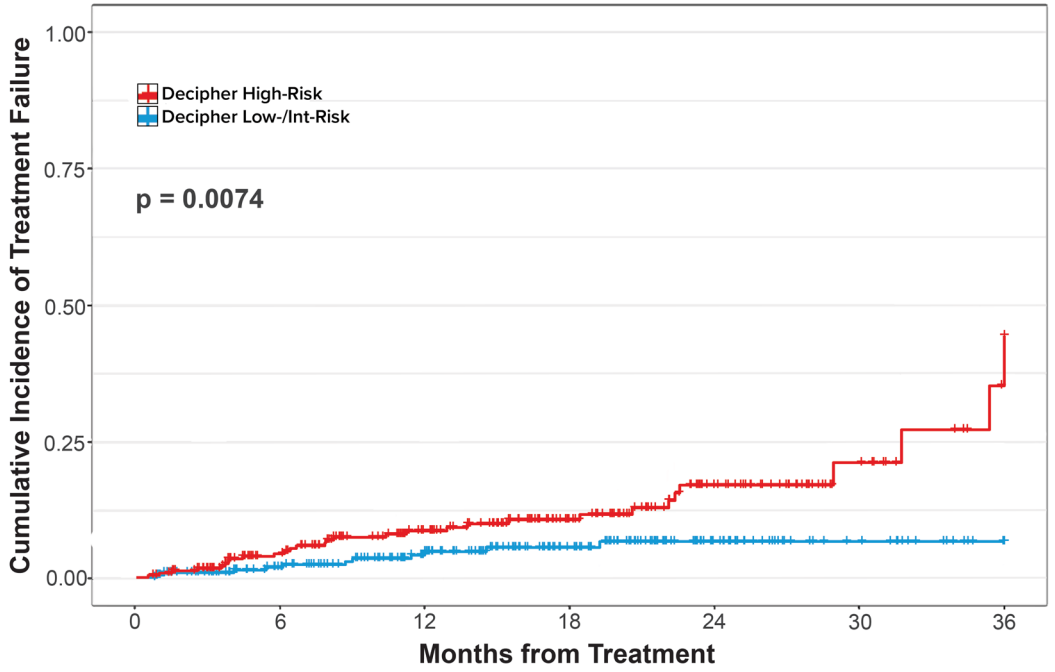
Vince Jr. et al., 2021
Prostate Cancer Prostatic Dis.

Michigan Urological Surgery Improvement Collaborative (MUSIC)

Active Surveillance: Time to Treatment



Definitive Therapy: Time to Treatment Failure



Decipher low-int.-risk men stay on active surveillance over **2x longer** than Decipher high-risk men.

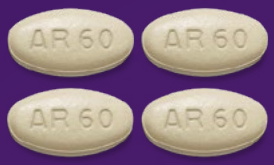
Decipher high-risk men had a **3x greater** rate of treatment failure* at 24 months (18%) compared with Decipher low- / int.-risk men (6%).

*Treatment failure= biochemical recurrence or receipt of salvage therapy

DOSING AND ADMINISTRATION

Erleada® (apalutamide) 60 mg tablets

ERLEADA® offers once-daily oral dosing[1]



Tablets shown are not actual size.

The recommended dose of ERLEADA® is 240 mg (four 60 mg tablets) administered **ORALLY ONCE DAILY**[1]

Patients should also receive a GnRH analog concurrently or should have had a bilateral orchiectomy.[1]

No need for co-administration of corticosteroid.[1]

Can be taken with or without food. Tablets should be swallowed whole.[1]

No initial dose adjustments for ERLEADA® are necessary for mild to moderate renal or hepatic impairment.[1] **ERLEADA® has not been evaluated in patients with severe renal or hepatic impairment.**

Dose modifications

- If a patient experiences a ≥Grade 3 toxicity or an intolerable side effect, hold dosing until symptoms improve to ≤Grade 1 or original grade, and then resume at the same dose or a reduced dose (180 mg or 120 mg), if warranted[1]

GnRH = gonadotropin-releasing hormone.

Learn about an alternate way to take ERLEADA®

- For patients who have difficulty swallowing tablets, ERLEADA® may be taken by mixing the tablets in applesauce. Please see Section 2.3 of the full Prescribing Information for ERLEADA® to learn more about this alternate method of administration

INDICATION

ERLEADA® (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with:

- Metastatic castration-sensitive prostate cancer (mCSPC)
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Cerebrovascular and Ischemic Cardiovascular Events — In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA® and 3% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA® and 2% of patients treated with placebo. Across the SPARTAN and TITAN studies, 5 patients (0.5%) treated with ERLEADA® and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event.

Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, or transient ischemic attack within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

In the SPARTAN study, cerebrovascular events occurred in 4.7% of patients treated with ERLEADA® and 0.8% of patients treated with placebo. In the TITAN study, cerebrovascular events occurred in 1.9% of patients treated with ERLEADA® and 2.1% of patients treated with placebo. Across the SPARTAN and TITAN studies, 3 patients (0.2%) treated with ERLEADA®, and 2 patients (0.2%) treated with placebo died from a cerebrovascular event.

Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA® for Grade 3 and 4 events.

Please see page 2 for additional Important Safety Information that includes information about drug interactions and see the full Prescribing Information for ERLEADA®.

Erleada® (apalutamide) 60 mg tablets

IMPORTANT SAFETY INFORMATION (continued)

Fractures — In a randomized study (SPARTAN) of patients with nmCRPC, fractures occurred in 12% of patients treated with ERLEADA® and in 7% of patients treated with placebo. In a randomized study (TITAN) of patients with mCSPC, fractures occurred in 9% of patients treated with ERLEADA® and in 6% of patients treated with placebo. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

Falls — In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA® compared with 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Falls occurred in patients receiving ERLEADA® with increased frequency in the elderly. Evaluate patients for fall risk.

Seizure — In two randomized studies (SPARTAN and TITAN), 5 patients (0.4%) treated with ERLEADA® and 1 patient treated with placebo (0.1%) experienced a seizure. Permanently discontinue ERLEADA® in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA®. Advise patients of the risk of developing a seizure while receiving ERLEADA® and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA® have not been established in females. Based on its mechanism of action, ERLEADA® can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA® *[see Use in Specific Populations (8.1, 8.3)]*.

ADVERSE REACTIONS

Adverse Reactions — The most common adverse reactions (≥10%) that occurred more frequently in the ERLEADA®-treated patients (≥2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Laboratory Abnormalities — All Grades (Grade 3-4)

- **Hematology** — In the TITAN study: white blood cell decreased ERLEADA® 27% (0.4%), placebo 19% (0.6%). In the SPARTAN study: anemia ERLEADA® 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA® 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA® 41% (2%), placebo 21% (2%)
- **Chemistry** — In the TITAN study: hypertriglyceridemia ERLEADA® 17% (3%), placebo 12% (2%). In the SPARTAN study: hypercholesterolemia ERLEADA® 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA® 70% (2%), placebo 59% (1%); hypertriglyceridemia ERLEADA® 67% (2%), placebo 49% (0.8%); hyperkalemia ERLEADA® 32% (2%), placebo 22% (0.5%)

Rash — In 2 randomized studies (SPARTAN and TITAN), rash was most commonly described as macular or maculopapular. Adverse reactions of rash were 26% with ERLEADA® vs 8% with placebo. Grade 3 rashes (defined as covering >30% body surface area [BSA]) were reported with ERLEADA® treatment (6%) vs placebo (0.5%).

The onset of rash occurred at a median of 83 days. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines, topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA®.

Hypothyroidism — In 2 randomized studies (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA® and 2% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA® and 7% of patients treated with placebo. The median onset was at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose-adjusted.

DRUG INTERACTIONS

Effect of Other Drugs on ERLEADA® — Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties. No initial dose adjustment is necessary; however, reduce the ERLEADA® dose based on tolerability *[see Dosage and Administration (2.2)]*.

Effect of ERLEADA® on Other Drugs

CYP3A4, CYP2C9, CYP2C19, and UGT Substrates — ERLEADA® is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA® with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is continued. Concomitant administration of ERLEADA® with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA® and evaluate for loss of activity.

P-gp, BCRP, or OATP1B1 Substrates — Apalutamide is a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of ERLEADA® with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP, or OATP1B1 must be co-administered with ERLEADA® and evaluate for loss of activity if medication is continued.

cp-50507v3

Please see the full Prescribing Information for ERLEADA®.

Reference: 1. ERLEADA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Janssen Biotech, Inc.

janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Visit erleadahcp.com

As soon as you diagnose mCSPC or nmCRPC

START EARLY WITH ERLEADA® (apalutamide)

TO PUSH BACK ON PROGRESSION

START EARLY WITH ERLEADA® TO GIVE YOUR PATIENTS A CHANCE TO LIVE LONGER

PROVEN EFFICACY[1,2]

TITAN study in mCSPC (dual primary endpoint)*:

FIRST AND ONLY

AR inhibitor to achieve a **35%** reduction in the risk of death in a registration trial in mCSPC

- (Median OS: NR vs 52.2 months; HR=0.65; 95% CI: 0.53, 0.79; *P*<0.0001; median follow-up time for final analysis: 44.0 months)[†2]
- (Median OS: NE vs NE; HR=0.67; 95% CI: 0.51, 0.89; *P*=0.0053; median follow-up time for primary analysis: 22.7 months)

SPARTAN study in nmCRPC (primary endpoint)[‡]:

FIRST AND ONLY

AR inhibitor to improve median MFS by **2 YEARS** in nmCRPC

- (40.5 months vs 16.2 months; HR=0.28; 95% CI: 0.23, 0.35; *P*<0.0001; median follow-up time for primary analysis: 20.3 months)[1,4]

TITAN study in mCSPC (dual primary endpoint)*:

ERLEADA® + ADT reduced the risk of radiographic progression or death by **52%** vs placebo + ADT

- (Median rPFS NE vs 22.1 months; HR=0.48; 95% CI: 0.39, 0.60; *P*<0.0001; median follow-up time for primary analysis: 22.7 months)[1,3]

SPARTAN study in nmCRPC (secondary endpoint)[‡]:

FIRST AND ONLY

therapy to improve median OS by **14 MONTHS** in nmCRPC

- (73.9 months; [6.2 years] vs 59.9 months [5 years]; HR=0.78; 95% CI: 0.64, 0.96; *P*=0.0161; median follow-up time for final analysis: 52.0 months)[1,5]

ESTABLISHED SAFETY PROFILE[1]

- In 2 pivotal trials that included a total of more than 2000 patients, the rate of serious adverse reactions with ERLEADA® + ADT was comparable with placebo + ADT[1]
  - TITAN Study: 20% ERLEADA® + ADT vs 20% placebo + ADT[1]
  - SPARTAN Study: 25% ERLEADA® + ADT vs 23% placebo + ADT[1]

NO NEGATIVE IMPACT TO HRQoL

(exploratory endpoint)[§6,7]

- In the TITAN study, HRQoL was maintained with ERLEADA® + ADT after a median follow-up of 44 months. Analysis of change from baseline in the FACT-P total score showed no substantial between-group differences[2]
- In the SPARTAN study, HRQoL was maintained with ERLEADA® + ADT after a median follow-up of 52 months. In patients receiving placebo + ADT, HRQoL declined after approximately 1 year[8]

BROAD ACCESS[9]

ERLEADA® is covered for 95% of Medicare Part D patients and 78% of commercial patients.[‖,9,10]

*All patients who enrolled in the TITAN study started ADT for mSCPC ≤6 months prior to randomization.[3]

[†]**TITAN final analysis data are not currently reported in the ERLEADA® Prescribing Information.**

[‡]In the SPARTAN study, conventional imaging (technetium-99m bone scans and CT scans) was used to confirm that patients were non-metastatic at screening for inclusion. Patients with pelvic lymph nodes <2 cm in short axis (N1) located below the iliac bifurcation at screening were allowed in the study. All patients in SPARTAN had a PSA doubling time ≤10 months in study entry.[1,4]

[§]The HRQoL analyses are not in the ERLEADA® Prescribing Information.

[‖]Prior authorization to label required for most plans.

ADT = androgen deprivation therapy; AR = androgen receptor; CI = confidence interval; CT = computed tomography; FACT-P = Functional Assessment of Cancer Therapy-Prostate; HR = hazard ratio; HRQoL = health-related quality of life; MFS = metastasis-free survival; mCSPC = metastatic castration-sensitive prostate cancer; MMIT = Managed Markets Insights & Technology; NE = non-estimable; nmCRPC = non-metastatic castration-resistant prostate cancer; NR = not reached; OS = overall survival; PSA = prostate-specific antigen; rPFS = radiographic progression-free survival; SPARTAN = Selective Prostate Androgen Receptor Targeting with ARN-509; TITAN = Targeted Investigational Treatment Analysis of Novel Antiandrogen.

INDICATIONS

ERLEADA® (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with:

- Metastatic castration-sensitive prostate cancer (mCSPC)
- Non-metastatic castration-resistant prostate cancer (nmCRPC)

IMPORTANT SAFETY INFORMATION

- Warnings and Precautions include cerebrovascular and ischemic cardiovascular events, fractures, falls, seizure, and embryo-fetal toxicity
- The most common adverse reactions (≥10%) that occurred more frequently in the ERLEADA®-treated patients (≥2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture

Please see Important Safety Information inside and the full Prescribing Information for ERLEADA®.

Erleada® (apalutamide) 60 mg tablets

As soon as you diagnose mCSPC or nmCRPC

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TO PUSH BACK ON PROGRESSION

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Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA® for Grade 3 and 4 events.

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Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA® have not been established in females. Based on its mechanism of action, ERLEADA® can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA® *[see Use in Specific Populations (8.1, 8.3)]*.

ADVERSE REACTIONS

Adverse Reactions — The most common adverse reactions (≥10%) that occurred more frequently in the ERLEADA®-treated patients (≥2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Laboratory Abnormalities — All Grades (Grade 3-4)

- **Hematology** — In the TITAN study: white blood cell decreased ERLEADA® 27% (0.4%), placebo 19% (0.6%). In the SPARTAN study: anemia ERLEADA® 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA® 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA® 41% (2%), placebo 21% (2%)
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IMPORTANT SAFETY INFORMATION (CONT´D)

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DRUG INTERACTIONS

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Effect of ERLEADA® on Other Drugs

CYP3A4, CYP2C9, CYP2C19, and UGT Substrates — ERLEADA® is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA® with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is continued. Concomitant administration of ERLEADA® with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA® and evaluate for loss of activity.

P-gp, BCRP, or OATP1B1 Substrates — Apalutamide is a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of ERLEADA® with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP, or OATP1B1 must be co-administered with ERLEADA® and evaluate for loss of activity if medication is continued.

cp-50507v3

Please click to see the full Prescribing Information for ERLEADA®.

References: 1. ERLEADA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Chi KN, Chowdhury S, Bjartell A, et al. Apalutamide in patients with metastatic, castration-sensitive prostate cancer: final survival analysis of the randomized, double-blind, phase III TITAN study [published online April 29, 2021]. *J Clin Oncol*. doi.org/10.1200/JCO.20.03488 **3.** Chi KN, Agarwal N, Bjartell A, et al; for the TITAN Investigators. Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med*. 2019;381(1):13-24. **4.** Smith MR, Saad F, Chowdhury S, et al; for the SPARTAN Investigators. Apalutamide treatment and metastasis-free survival in prostate cancer. *N Engl J Med*. 2018;378(15):1408-1418. **5.** Smith MR, Saad F, Chowdhury S, et al. Apalutamide and overall survival in prostate cancer. *Eur Urol.* 2021;79(1):150-158. **6.** Agarwal N, McQuarrie K, Bjartell A, et al; TITAN Investigators. Health-related quality of life after apalutamide treatment in patients with metastatic castration-sensitive prostate cancer (TITAN): a randomised, placebo-controlled, phase 3 study. *Lancet Oncol*. 2019;20(11):1518-1530. **7.** Saad F, Cella D, Basch E, et al. Effect of apalutamide on health-related quality of life in patients with non-metastatic castration-resistant prostate cancer: an analysis of the SPARTAN randomised, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2018;19(10):1404-1416. **8.** Oudard S, Hadaschik B, Saad F, et al. Health-related quality of life at final analysis of the SPARTAN study of apalutamide vs placebo in patients with nonmetastatic castration-resistant prostate cancer receiving androgen deprivation therapy. Poster presented at: ESMO Virtual Congress; September 18-22, 2020. **9.** MMIT; February 2021. **10.** Data on file. Janssen Biotech, Inc. Date of data July 2021. Date information was collected June 2021.

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