PATIENT CASE*

Germline BRCA1/2 negative mCRPC patient underwent PSMA-PET imaging to guide subsequent treatment after JEVTANA® (cabazitaxel)

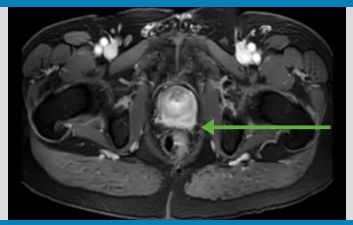
*Case report is based on a de-identified actual patient of Pedro Barata, MD, MSc†

Mike, 73 years old
(patient portrayal)

Presentation and Work-up Results

Progressive urinary difficulty and nocturia

Father had prostate cancer



Prostate MRI revealed PI-RADS 5 lesion on the left prostate gland

MRI fusion biopsy reveals Gleason 5+5=10; prostate adenocarcinoma

High volume with extracapsular and nodal involvement

PSA 13.1 ng/mL

Initial Management (27 months)

Systemic ADT

EBRT to pelvic lymph nodes, prostate, and seminal vesicles

1.5 year later biopsy of neck lymph node shows metastatic prostate carcinoma

Bicalutamide initiated

PSA rose from 3 ng/mL to10 ng/mL, despite castrate testosterone levels of 0.75 ng/dL

Within 3 months, post-bicalutamide scans showed disease progression with bone and lymph nodes

ADT=androgen deprivation therapy; EBRT=external beam radiation therapy; mCRPC=metastatic castration-resistant prostate cancer; MRI=magnetic resonance imaging; PI-RADS=prostate imaging reporting and data system; PSA=prostate-specific antigen.
† Dr. Barata was compensated and/or received an honorarium from Sanofi in connection with this material.

INDICATION

JEVTANA is a microtubule inhibitor indicated in combination with prednisone for treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) previously treated with a docetaxel-containing treatment regimen.

IMPORTANT SAFETY INFORMATION

WARNING: NEUTROPENIA AND HYPERSENSITIVITY

Neutropenia: Neutropenic deaths have been reported. Monitor for neutropenia with frequent blood cell counts. JEVTANA is contra-indicated in patients with neutrophil counts of ≤1,500 cells/mm^3. Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features. Consider primary prophylaxis with G-CSF in all patients receiving a dose of 25 mg/m^2.

Severe hypersensitivity: Severe hypersensitivity reactions can occur and may include generalized rash/erythema, hypotension and bronchospasm. Severe hypersensitivity reactions require immediate discontinuation of the JEVTANA infusion and administration of appropriate therapy. Patients should receive premedication. JEVTANA is contraindicated in patients who have a history of severe hypersensitivity reactions to cabazitaxel or to other drugs formulated with polysorbate 80.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

JEVTANA® (cabazitaxel) injection

Mike's treatment journey in mCRPC

Docetaxel + Prednisone — 9 months

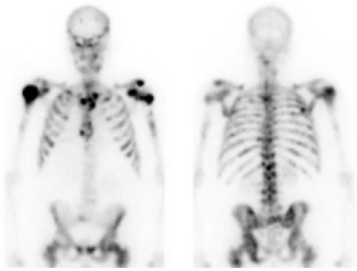
Patient received 9 cycles of docetaxel (75 mg/m^2 Q3W) + prednisone

AEs included:
- **Grade 1** neuropathy
- **Grade 1** asthenia

Patient experienced rising calcium levels and continued taking denosumab

PSA 28.33 ng/mL

1 month after the last docetaxel cycle, scans showed disease progression with new bony lesions



Abiraterone + Prednisone — 16 months

Patient continued therapy for 16 months with PSA nadir 1.8 ng/mL

AEs included:
- Mild pain in lower back and leg
- **Grade 2** fatigue
- **Grade 1** hypokalemia
- **Grade 1** hypertension

PSA 7.48 ng/mL

Enlarged lymph nodes and 3 more bony lesions found on restaging scans

Negative germline test

JEVTANA® (cabazitaxel) + Prednisone — 9 months

JEVTANA (20 mg/m^2 Q3W) + prednisone 10 mg QD initiated; 10 cycles completed

PSA nadir 1.3 ng/mL

AEs included:
- **Grade 1** neuropathy
- **Grade 1** fatigue
- **Grade 1** cytopenia

At cycle 7, CT and bone scan showed sclerotic lesions in the left lateral scapula; osseous metastases

3 months after last JEVTANA cycle, PSA 3.57 ng/mL

Lutetium — 4 months

PSMA-PET revealed multiple enlarged left supraclavicular cervical lymph nodes, retroperitoneal lymph nodes periaortic, retrocrural, and left common iliac chains left lateral scapula

AEs included:
- **Grade 1** thrombocytopenia
- **Grade 1** dry mouth

Received 3 cycles of lutetium 177-PSMA-617 with more planned

*ADT (androgen deprivation therapy) maintained throughout mCRPC treatment regimens.

AE=adverse event; CT=computerized tomography; mCRPC=metastatic castration-resistant prostate cancer; PSA=prostate-specific antigen; PSMA-PET=prostate-specific membrane antigen positron emission tomography; Q3W=every 3 weeks; QD=once daily.

IMPORTANT SAFETY INFORMATION – cont'd

CONTRAINDICATIONS

JEVTANA is contraindicated in patients with neutrophil counts of ≤1,500/mm^3, patients with a history of severe hypersensitivity reactions to cabazitaxel or to other drugs formulated with polysorbate 80, and patients with severe hepatic impairment (total bilirubin >3x upper limit of normal (ULN)).

WARNINGS AND PRECAUTIONS

Bone Marrow Suppression (BMS): BMS manifested as neutropenia, anemia, thrombocytopenia and/or pancytopenia may occur. Neutropenic deaths have been reported. Monitor blood counts frequently to determine if initiation of G-CSF and/or dosage modification is needed. Monitoring of complete blood counts is essential on a weekly basis during cycle 1 and before each treatment cycle thereafter so that the dose can be adjusted, if needed. Caution is recommended in patients with hemoglobin <10 g/dl.

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JEVTANA® (cabazitaxel) injection

JEVTANA® (cabazitaxel) has been studied in the CARD trial

CARD: The first comparative, prospective, phase 4 trial evaluated JEVTANA vs ARPI in mCRPC patients who had previously received a docetaxel-containing regimen[1]

Randomized, open-label, multicenter trial (N=255)

Patients with mCRPC† who had previously received docetaxel (at least 3 cycles before or after abiraterone or enzalutamide) and had disease progression within 12 months on abiraterone or enzalutamide

DOCE ▶ ARPI

OR

ARPI ▶ DOCE

Stratification:
- ECOG PS: 0,1 vs 2
- Time to disease progression (≤6 months vs >6 to 12 months)
- Timing of previous treatment with abiraterone or enzalutamide (before vs after docetaxel)

Randomized

JEVTANA 25 mg/m² q3w + oral prednisone 10 mg daily + G-CSF (n=129)

Oral abiraterone 1000 mg once daily + oral prednisone 5 mg twice daily OR oral enzalutamide 160 mg once daily (n=126)‡

- **Primary endpoint:** radiographic progression-free survival (rPFS*)
- **Secondary endpoints:** overall survival (OS), tumor response, and safety

*rPFS is defined as the time from randomization to the occurrence of one of the following events: radiological tumor progression using RECIST 1.1 (except for lymph nodes: if lymph node metastasis is the only evidence of metastasis at baseline, it must be ≥20 mm in diameter when measured by spiral CT or MRI [as defined by PCWG2]), progression of bone lesions according to PCWG2 criteria, or death.[5]

ARPI=AR Pathway Inhibitor (abiraterone or enzalutamide); CT=computed tomography; DOCE=docetaxel; ECOG PS=Eastern Cooperative Oncology Group performance status; G-CSF=granulocyte-colony stimulating factor; MRI=magnetic resonance imaging; PCWG2=Prostate Cancer Clinical Trials Working Group 2; q3w=every 3 weeks; RECIST=Response Evaluation Criteria in Solid Tumors.

†Patients had histologically confirmed prostate cancer and castrate levels of serum testosterone (<0.5 ng/mL).[2]

‡Abiraterone was given to patients who had previously received enzalutamide before trial entry and enzalutamide was given to patients who had previously received abiraterone.[2]

IMPORTANT SAFETY INFORMATION – cont'd

WARNINGS AND PRECAUTIONS – cont'd

Increased Toxicities in Elderly Patients: Patients ≥65 years of age were more likely to experience fatal outcomes not related to disease progression and certain adverse reactions, including neutropenia and febrile neutropenia. Monitor closely.

Hypersensitivity Reactions: Severe hypersensitivity reactions can occur. Premedicate all patients with antihistamines, corticosteroids and H_2 antagonists prior to JEVTANA. Observe patients closely, especially during the first and second infusions. Discontinue JEVTANA immediately if severe hypersensitivity occurs and treat as indicated.

Gastrointestinal (GI) Adverse Reactions: Nausea, vomiting, and severe diarrhea may occur. Death related to diarrhea and electrolyte imbalance occurred in the randomized clinical trials and mortality related to diarrhea has been reported. Intensive measures may be required for severe diarrhea and electrolyte imbalance. Rehydrate and treat with antiemetics and antidiarrheals as needed. If experiencing grade ≥3 diarrhea, dosage should be modified.

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JEVTANA® (cabazitaxel) injection

Efficacy

2X rPFS

PRIMARY ENDPOINT (ITT population)

Doubled median rPFS

JEVTANA median rPFS **8.0 months** [95% CI: 5.7-9.2] (n=129) vs ARPI median rPFS **3.7 months** [95% CI: 2.8-5.1] (n=126). *P<0.0001,* HR=0.54 (95% CI, 0.40–0.73)

All efficacy analyses were performed on the Intent to Treat (ITT) population, at the cutoff date for 196 rPFS events.

36% relative reduction in risk of death

SECONDARY ENDPOINT (ITT population)

Significantly improved median OS

JEVTANA median OS **13.6 months** [95% CI: 11.5-17.5] (n=129) vs ARPI median OS **11.0 months** [95% CI: 9.2-12.9] (n=126), *P*=0.008, HR=0.64 (95% CI: 0.46-0.89)

At the cutoff date, 153 deaths were noted with 70 deaths (54.3%) occurring in the JEVTANA 25 mg/m^2 group and 83 (65.9%) in the ARPI group.

≥30% tumor reduction in 3X more patients

SECONDARY ENDPOINT (Patients with measurable disease at baseline)

Tumor response

JEVTANA **36.5%** tumor response (23 of 63 patients) [95% CI: 26.6-48.4] vs ARPI **11.5%** tumor response (6 of 52 patients) [95% CI: 2.9-20.2], *P*=0.004

Partial Response was measured by RECIST criteria, which is defined a at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters.

ARPI=AR Pathway Inhibitor

IMPORTANT SAFETY INFORMATION – cont'd

WARNINGS AND PRECAUTIONS – cont'd

Gastrointestinal (GI) Adverse Reactions – cont'd: GI hemorrhage and perforation, ileus, enterocolitis, neutropenic enterocolitis, including fatal outcome, have been reported. Risk may be increased with neutropenia, age, steroid use, concomitant use of NSAIDs, antiplatelet therapy or anticoagulants, and prior history of pelvic radiotherapy, adhesions, ulceration and GI bleeding. Abdominal pain and tenderness, fever, persistent constipation, diarrhea, with or without neutropenia, may be early manifestations of serious GI toxicity and should be evaluated and treated promptly. JEVTANA treatment delay or discontinuation may be necessary.

Renal Failure: Cases, including those with fatal outcomes, have been reported. Identify cause and manage aggressively.

Urinary Disorders including Cystitis: Cystitis, radiation cystitis, and hematuria, including that requiring hospitalization, has been reported with JEVTANA in patients who previously received pelvic radiation. Cystitis from radiation recall may occur late in treatment with JEVTANA. Monitor patients who previously received pelvic radiation for signs and symptoms of cystitis while on JEVTANA. Interrupt or discontinue JEVTANA in patients experiencing severe hemorrhagic cystitis. Medical and/or surgical supportive treatment may be required to treat severe hemorrhagic cystitis.

Respiratory Disorders: Interstitial pneumonia/pneumonitis, interstitial lung disease and acute respiratory distress syndrome have been reported and may be associated with fatal outcome. Patients with underlying lung disease may be at higher risk for these events. Acute respiratory distress syndrome may occur in the setting of infection. Interrupt JEVTANA if new or worsening pulmonary symptoms develop. Closely monitor, promptly investigate, and appropriately treat patients receiving JEVTANA. Consider discontinuation. The benefit of resuming JEVTANA treatment must be carefully evaluated.

Use in Patients with Hepatic Impairment: JEVTANA dose should be reduced for patients with mild (total bilirubin >1 to ≤1.5 x ULN or AST >1.5 x ULN) and moderate (total bilirubin >1.5 to ≤3.0 x ULN and any AST) hepatic impairment, based on tolerability data in these patients. Administer JEVTANA 20 mg/m^2 for mild hepatic impairment. Administer JEVTANA 15 mg/m^2 for moderate hepatic impairment. Monitor closely.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

JEVTANA® (cabazitaxel) injection

Safety

- No New Safety Signals Were Observed[2]
- ARs of grade ≥3 occurred at similar rates for men receiving Jevtana as those receiving abiraterone or enzalutamide (56.3% vs 52.4%)

ARs* and Hematologic Abnormalities in ≥5% of Patients in the CARD Trial[1]

G-CSF was mandated every cycle per trial protocol. Per the full Prescribing Information, primary prophylaxis is recommended in patients with high-risk clinical features.

	JEVTANA 25 mg/m² + prednisone/prednisolone + G-CSF (n=126)	abiraterone + prednisone/ prednisolone or enzalutamide (n=124)
Adverse reactions	**Grade 3–4**	
Anemia†	8%	4.8%
Lymphopenia†	27%	17%
Neutropenia†	45%	3.2%
Thrombocytopenia†	3.2%	1.6%
Fatigue‡	4%	2.4%
Edema peripheral§	0.8%	1.6%
Pyrexia	0	0
Pain	0	0.8%
Diarrhea¶	4.8%	0
Nausea	0	0.8%
Constipation	0	0
Abdominal pain#	1.6%	0.8%
Vomiting	0	1.6%
Stomatitis	0	0
Dyspepsia	0	0
Musculoskeletal pain**	1.6%	6%
Pain in extremity	0	2.4%
Bone fracture††	1.6%	2.4%
Infections‡‡	4%	6%

	JEVTANA 25 mg/m² + prednisone/prednisolone + G-CSF (n=126	abiraterone + prednisone/ prednisolone or enzalutamide (n=124)
Adverse reactions	**Grade 3–4**	
Peripheral neuropathy§§	1.6%	0
Dysgeusia	0	0
Polyneuropathy	1.6%	0
Dizziness	0	0
Hematuria¶¶	0.8%	1.6%
Lower urinary tract symptoms##	0	0
Acute kidney injury***	2.4%	4%
Decreased appetite	0.8%	2.4%
Hypokalemia	0	0
Cancer pain	1.6%	2.4%
Cardiac disorders†††	0.8%	3.2%
Pneumonia‡‡‡	1.6%	0.8%
Dyspnea	0	0
Alopecia	0	0
Fall	0	0
Hypertension§§§	2.4%	2.4%
Weight decreased	0	0
Insomnia	0	0

ARs=adverse reactions.

* Grade from NCI CTCAE version 4.0.

† Based on laboratory values -% calculated using the number of patients with at least one event(n) over the number of patients assessed for each parameter during the on-treatment period.

‡ Includes asthenia, fatigue, lethargy, malaise.

§ Includes lymphoedema, edema peripheral, peripheral swelling.

¶ Includes colitis, diarrhea, diarrhea hemorrhagic, gastroenteritis.

Includes abdominal pain, abdominal pain lower, abdominal pain upper, flank pain, gastrointestinal pain.

** Includes arthralgia, back pain, bone pain, musculoskeletal chest pain, musculoskeletal discomfort, musculoskeletal pain, myalgia, neck pain, noncardiac chest pain.

†† Includes femoral neck fracture, pathological fracture, rib fracture, spinal compression fracture, sternal fracture, thoracic vertebral fracture.

‡‡ Includes bacteremia, bacteriuria, cellulitis, device related sepsis, Enterobacter sepsis, erysipelas, furuncle, influenza, influenza like illness, localized infection, oral fungal infection, perineal cellulitis, pulmonary sepsis, pyelocalliectasis, pyelonephritis, pyelonephritis acute, respiratory tract infection, respiratory tract infection viral, sepsis, septic shock, subcutaneous abscess, upper respiratory tract infection, ureteritis, urinary tract infection, urinary tract infection bacterial, urosepsis, viral infection.

§§ Includes neuropathy peripheral, paresthesia, peripheral motor neuropathy, peripheral sensorimotor neuropathy, peripheral sensory neuropathy.

¶¶ Includes hematuria, cystitis hemorrhagic.

Includes lower urinary tract symptoms, micturition urgency, nocturia, pollakiuria, urinary incontinence, urinary retention, dysuria.

*** Includes acute kidney injury, blood creatinine increased, renal failure, renal impairment.

††† Includes aortic valve incompetence, aortic valve stenosis, atrial fibrillation, atrial flutter, atrioventricular block complete, atrioventricular block second degree, bradycardia, sinus bradycardia, tachycardia, cardiac failure, acute coronary syndrome, angina pectoris.

‡‡‡ Includes lower respiratory tract infection, lung infection, lung infiltration, pneumonia.

§§§ Includes hypertension, hypertensive crisis.

JEVTANA® (cabazitaxel) injection

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

Cabazitaxel (JEVTANA) Is a National Comprehensive Cancer Network® (NCCN®) Designated Category 1* Option for mCRPC Patients After Docetaxel and a Novel Hormonal Therapy[2]

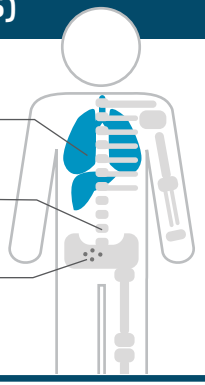
JEVTANA is a proven option for your patients with mCRPC after a docetaxel containing regimen

JEVTANA has been studied in over 2,200 mCRPC patients across 2 phase 3 trials and 1 phase 4 trial, including men with a high disease burden who were age ≥75 years

TROPIC[3,4] Study (n=755)

Disease burden:

- Visceral 25%
- Bone 84%
- Distant Lymph Nodes 35%

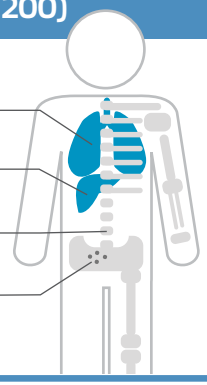


45% had pain at baseline

PROSELICA[3,5] Study (n=1200)

Disease burden:

- Lung 16%
- Liver 15%
- Bone 94%
- Distant Lymph Nodes 49%

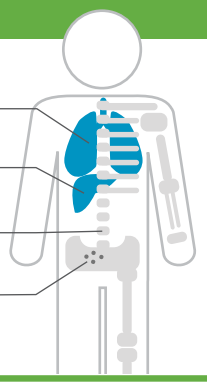


44% had pain at baseline

CARD[1,3] Study (n=255)

Disease burden:

- Lung 7%
- Liver 11%
- Bone (+/- lymph nodes) 59%
- Lymph Nodes 5%



69% had pain at baseline

* The noted category applies only if there are no visceral metastases.

IMPORTANT SAFETY INFORMATION – cont'd

WARNINGS AND PRECAUTIONS – cont'd

Embryo-Fetal Toxicity: JEVTANA can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of JEVTANA.

ADVERSE REACTIONS (ARs)

The most common all grades adverse reactions and laboratory abnormalities (≥10%) with JEVTANA 20 mg/m^2 or 25 mg/m^2 are neutropenia, anemia, diarrhea, nausea, fatigue, asthenia, vomiting, hematuria, constipation, decreased appetite, back pain, and abdominal pain.

DRUG INTERACTIONS

Avoid coadministration of JEVTANA with strong CYP3A inhibitors. If patients require coadministration of a strong CYP3A inhibitor, consider a 25% JEVTANA dose reduction.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** The safety and efficacy of JEVTANA have not been established in females. There are no human data on the use of JEVTANA in pregnant women to inform the drug-associated risk.
- **Lactation:** The safety and efficacy of JEVTANA have not been established in females. There is no information available on the presence of JEVTANA in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production.
- **Females and Males of Reproductive Potential:** Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of JEVTANA.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

References: 1. de Wit R, de Bono J, Sternberg CN, et al; for the CARD Investigators. Cabazitaxel versus abiraterone or enzalutamide in metastatic prostate cancer. *N Engl J Med.* 2019;381(26):2506-2518. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer, V.1.2023. ©National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed Aug. 24th, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** JEVTANA Prescribing Information. Bridgewater, NJ: sanofi-aventis U.S. LLC. **4.** de Bono JS, Oudard S, Ozguroglu M, et al; for the TROPIC Investigators. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomized open-label trial. *Lancet.* 2010;376(9747): 1147-1154. **5.** Eisenberger M, Hardy-Bessard AC, Kim CS, et al. Phase III study comparing a reduced dose of cabazitaxel (20 mg/m^2) and the currently approved dose (25 mg/m^2) in post docetaxel patients with metastatic castration-resistant prostate cancer–PROSELICA. *J Clin Oncol.* 2017;35:1-13.

JEVTANA® (cabazitaxel) injection

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