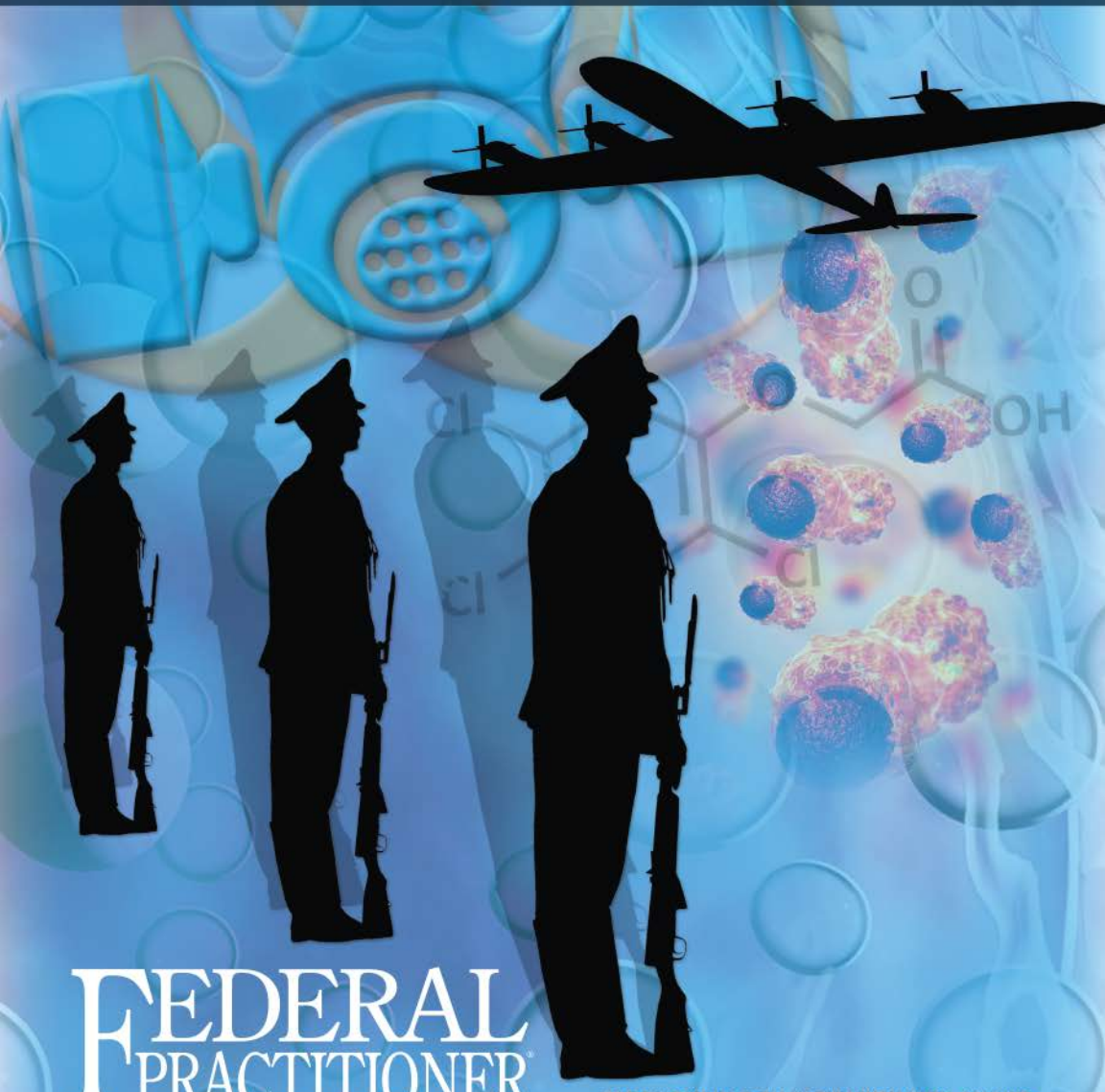
A FEDERAL PRACTITIONER® EXCLUSIVE

CANCER DATA TRENDS 2020



FEDERAL PRACTITIONER®

PRODUCED IN COLLABORATION WITH AVAHO

IN THE MARATHON OF MYELOMA TREATMENT,

ARE YOU DROPPING THE PROTEASOME INHIBITOR TOO SOON?

Continuous treatment with a proteasome inhibitor (PI)–based regimen is associated with clinical benefits, including for patients with high-risk cytogenetics.[1-3*] However, many patients who have had 1 prior therapy receive injectable PIs for only 4 to 7 months.[4,5]

The NINLARO® (ixazomib) regimen† extended median PFS by ~6 months (median: 20.6 vs 14.7 months) vs the placebo regimen† in patients with multiple myeloma who have received at least 1 prior therapy.[1‡]

Consider prescribing the all-oral NINLARO regimen for long-term§ proteasome inhibition.[6,7]

TOURMALINE-MM1: a global, phase 3, randomized (1:1), double-blind, placebo-controlled study that evaluated the safety and efficacy of NINLARO (an oral PI) vs placebo, both in combination with lenalidomide and dexamethasone, until disease progression or unacceptable toxicity in 722 patients with relapsed and/or refractory multiple myeloma who received 1-3 prior therapies.[1]

NINLARO is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Thrombocytopenia** has been reported with NINLARO. During treatment, monitor platelet counts at least monthly, and consider more frequent monitoring during the first three cycles. Manage thrombocytopenia with dose modifications and platelet transfusions as per standard medical guidelines. Adjust dosing as needed. Platelet nadirs typically occurred between Days 14-21 of each 28-day cycle and recovered to baseline by the start of the next cycle.
- **Gastrointestinal Toxicities**, including diarrhea, constipation, nausea and vomiting, were reported with NINLARO and may occasionally require the use of antidiarrheal and antiemetic medications, and supportive care. Diarrhea resulted in the discontinuation of one or more of the three drugs in 1% of patients in the NINLARO regimen and < 1% of patients in the placebo regimen. Adjust dosing for severe symptoms.
- **Peripheral Neuropathy** (predominantly sensory) was reported with NINLARO. The most commonly reported reaction was peripheral sensory neuropathy (19% and 14% in the NINLARO and placebo regimens, respectively). Peripheral motor neuropathy was not commonly reported in either regimen (< 1%). Peripheral neuropathy resulted in discontinuation of one or more of the three drugs in 1% of patients in both regimens. Monitor patients for symptoms of peripheral neuropathy and adjust dosing as needed.
- **Peripheral Edema** was reported with NINLARO. Monitor for fluid retention. Investigate for underlying causes when appropriate and provide supportive care as necessary. Adjust dosing of dexamethasone per its prescribing information or NINLARO for Grade 3 or 4 symptoms.
- **Cutaneous Reactions:** Rash, most commonly maculo-papular and macular rash, was reported with NINLARO. Rash resulted in discontinuation of one or more of the three drugs in < 1% of patients in both regimens. Manage rash with supportive care or with dose modification.
- **Thrombotic Microangiopathy:** Cases, sometimes fatal, of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), have been reported in patients who received NINLARO. Monitor for signs and symptoms of TTP/HUS. If the diagnosis is suspected, stop NINLARO and evaluate. If the diagnosis of TTP/HUS is excluded, consider restarting NINLARO. The safety of reinitiating NINLARO therapy in patients previously experiencing TTP/HUS is not known.
- **Hepatotoxicity** has been reported with NINLARO. Drug-induced liver injury, hepatocellular injury, hepatic steatosis, hepatitis cholestatic and hepatotoxicity have each been reported in < 1% of patients treated with NINLARO. Events of liver impairment have been reported (6% in the NINLARO regimen and 5% in the placebo regimen). Monitor hepatic enzymes regularly during treatment and adjust dosing as needed.
- **Embryo-fetal Toxicity:** NINLARO can cause fetal harm. Women should be advised of the potential risk to a fetus, to avoid becoming pregnant, and to use contraception during treatment and for an additional 90 days after the final dose of NINLARO. Women using hormonal contraceptives should also use a barrier method of contraception.

ADVERSE REACTIONS

The most common adverse reactions (≥ 20%) in the NINLARO regimen and greater than the placebo regimen, respectively, were diarrhea (42%, 36%), constipation (34%, 25%), thrombocytopenia (78%, 54%; pooled from adverse events and laboratory data), peripheral neuropathy (28%, 21%), nausea (26%, 21%), peripheral edema (25%, 18%), vomiting (22%, 11%), and back pain (21%, 16%). Serious adverse reactions reported in ≥ 2% of patients included thrombocytopenia (2%) and diarrhea (2%).

DRUG INTERACTIONS: Avoid concomitant administration of NINLARO with strong CYP3A inducers.

SPECIAL POPULATIONS

- **Hepatic Impairment:** Reduce the NINLARO starting dose to 3 mg in patients with moderate or severe hepatic impairment.
- **Renal Impairment:** Reduce the NINLARO starting dose to 3 mg in patients with severe renal impairment or end-stage renal disease requiring dialysis. NINLARO is not dialyzable.
- **Lactation:** Advise nursing women not to breastfeed during treatment with NINLARO and for 90 days after the last dose.

*Defined as patients with del(17p), t(4;14), and/or t(14;16).

†The NINLARO regimen included NINLARO+lenalidomide+dexamethasone. The placebo regimen included placebo+lenalidomide+dexamethasone.

‡95% CI, 17.0-NE and 95% CI, 12.9-17.6, respectively; HR=0.74 (95% CI, 0.59-0.94); *P*=0.012.

§**Defined as treatment to progression or unacceptable toxicity.**

NE=not evaluable; PFS=progression-free survival.

REFERENCES: 1. Moreau P, Masszi T, Grzasko N, et al; for TOURMALINE-MM1 Study Group. Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med.* 2016;374(17):1621-1634. **2.** Richardson PG, Laubach J, Gandolfi S, Facon T, Weisel K, O'Gorman P. Maintenance and continuous therapy for multiple myeloma. *Expert Rev Anticancer Ther.* 2018;18(8):751-764. **3.** Richardson PG, Zweegman S, O'Donnell EK, et al. Ixazomib for the treatment of multiple myeloma. *Expert Opin Pharmacother.* 2018;19(17):1949-1968. **4.** Hari P, Romanus D, Palumbo A, et al. Prolonged duration of therapy is associated with improved survival in patients treated for relapsed/refractory multiple myeloma in routine clinical care in the United States. *Clin Lymphoma Myeloma Leuk.* 2018;18(2):152-160. **5.** Jagannath S, Roy A, Kish J, et al. Real-world treatment patterns and associated progression-free survival in relapsed/refractory multiple myeloma among US community oncology practices. *Expert Rev Hematol.* 2016;9(7):707-717, Supplemental Table 2. https://www.tandfonline.com/doi/suppl/10.1080/17474086.2016.1195254?scroll=top. Accessed March 30, 2020. **6.** Revlimid [package insert]. Summit, NJ: Celgene Corp; 2019. **7.** Dexamethasone [package insert]. Columbus, OH: Roxane Laboratories, Inc; 2015.

Please see accompanying Brief Summary.

Takeda

NINLARO® (ixazomib) capsules
4mg | 3mg | 2.3mg

NINLARO (ixazomib) capsules
4mg | 3mg | 2.3mg

BRIEF SUMMARY OF PRESCRIBING INFORMATION
NINLARO (ixazomib) capsules, for oral use

1 INDICATION

NINLARO (ixazomib) is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

5 WARNINGS AND PRECAUTIONS

5.1 Thrombocytopenia: Thrombocytopenia has been reported with NINLARO with platelet nadirs typically occurring between Days 14-21 of each 28-day cycle and recovery to baseline by the start of the next cycle. Three percent of patients in the NINLARO regimen and 1% of patients in the placebo regimen had a platelet count ≤ 10,000/mm³ during treatment. Less than 1% of patients in both regimens had a platelet count ≤ 5000/mm³ during treatment. Discontinuations due to thrombocytopenia were similar in both regimens (< 1% of patients in the NINLARO regimen and 2% of patients in the placebo regimen discontinued one or more of the three drugs).The rate of platelet transfusions was 6% in the NINLARO regimen and 5% in the placebo regimen.

Monitor platelet counts at least monthly during treatment with NINLARO. Consider more frequent monitoring during the first three cycles. Manage thrombocytopenia with dose modifications and platelet transfusions as per standard medical guidelines.

5.2 Gastrointestinal Toxicities: Diarrhea, constipation, nausea, and vomiting, have been reported with NINLARO, occasionally requiring use of antidiarrheal and antiemetic medications, and supportive care. Diarrhea was reported in 42% of patients in the NINLARO regimen and 36% in the placebo regimen, constipation in 34% and 25%, respectively, nausea in 26% and 21%, respectively, and vomiting in 22% and 11%, respectively. Diarrhea resulted in discontinuation of one or more of the three drugs in 1% of patients in the NINLARO regimen and < 1% of patients in the placebo regimen. Adjust dosing for Grade 3 or 4 symptoms.

5.3 Peripheral Neuropathy: The majority of peripheral neuropathy adverse reactions were Grade 1 (18% in the NINLARO regimen and 14% in the placebo regimen) and Grade 2 (8% in the NINLARO regimen and 5% in the placebo regimen). Grade 3 adverse reactions of peripheral neuropathy were reported at 2% in both regimens; there were no Grade 4 or serious adverse reactions.

The most commonly reported reaction was peripheral sensory neuropathy (19% and 14% in the NINLARO and placebo regimen, respectively). Peripheral motor neuropathy was not commonly reported in either regimen (< 1%). Peripheral neuropathy resulted in discontinuation of one or more of the three drugs in 1% of patients in both regimens. Patients should be monitored for symptoms of neuropathy. Patients experiencing new or worsening peripheral neuropathy may require dose modification.

5.4 Peripheral Edema: Peripheral edema was reported in 25% and 18% of patients in the NINLARO and placebo regimens, respectively. The majority of peripheral edema adverse reactions were Grade 1 (16% in the NINLARO regimen and 13% in the placebo regimen) and Grade 2 (7% in the NINLARO regimen and 4% in the placebo regimen).

Grade 3 peripheral edema was reported in 2% and 1% of patients in the NINLARO and placebo regimens, respectively. There was no Grade 4 peripheral edema reported. There were no discontinuations reported due to peripheral edema. Evaluate for underlying causes and provide supportive care, as necessary. Adjust dosing of dexamethasone per its prescribing information or NINLARO for Grade 3 or 4 symptoms.

5.5 Cutaneous Reactions: Rash was reported in 19% of patients in the NINLARO regimen and 11% of patients in the placebo regimen. The majority of the rash adverse reactions were Grade 1 (10% in the NINLARO regimen and 7% in the placebo regimen) or Grade 2 (6% in the NINLARO regimen and 3% in the placebo regimen). Grade 3 rash was reported in 3% of patients in the NINLARO regimen and 1% of patients in the placebo regimen. There were no Grade 4 or serious adverse reactions of rash reported. The most common type of rash reported in both regimens included maculo-papular and macular rash. Rash resulted in discontinuation of one or more of the three drugs in < 1% of patients in both regimens. Manage rash with supportive care or with dose modification if Grade 2 or higher.

5.6 Thrombotic Microangiopathy: Cases, sometimes fatal, of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), have been reported in patients who received NINLARO. Monitor for signs and symptoms of TTP/HUS. If the diagnosis is suspected, stop NINLARO and evaluate. If the diagnosis of TTP/HUS is excluded, consider restarting NINLARO. The safety of reinitiating NINLARO therapy in patients previously experiencing TTP/HUS is not known.

5.7 Hepatotoxicity: Drug-induced liver injury, hepatocellular injury, hepatic steatosis, hepatitis cholestatic and hepatotoxicity have each been reported in < 1% of patients treated with NINLARO. Events of liver impairment have been reported (6% in the NINLARO regimen and 5% in the placebo regimen). Monitor hepatic enzymes regularly and adjust dosing for Grade 3 or 4 symptoms.

5.8 Embryo-Fetal Toxicity: NINLARO can cause fetal harm when administered to a pregnant woman based on the mechanism of action and findings in animals. There are no adequate and well-controlled studies in pregnant women using NINLARO. Ixazomib caused embryo-fetal toxicity in pregnant rats and rabbits at doses resulting in exposures that were slightly higher than those observed in patients receiving the recommended dose.

Females of reproductive potential should be advised to avoid becoming pregnant while being treated with NINLARO. If NINLARO is used during pregnancy or if the patient becomes pregnant while taking NINLARO, the patient should be apprised of the potential hazard to the fetus. Advise females of reproductive potential that they must use effective contraception during treatment with NINLARO and for 90 days following the final dose. Women using hormonal contraceptives should also use a barrier method of contraception.

6 ADVERSE REACTIONS

The following adverse reactions are described in detail in other sections of the prescribing information:

- Thrombocytopenia *[see Warnings and Precautions (5.1)]*
- Gastrointestinal Toxicities *[see Warnings and Precautions (5.2)]*
- Peripheral Neuropathy *[see Warnings and Precautions (5.3)]*
- Peripheral Edema *[see Warnings and Precautions (5.4)]*
- Cutaneous Reactions *[see Warnings and Precautions (5.5)]*
- Thrombotic Microangiopathy *[see Warnings and Precautions (5.6)]*
- Hepatotoxicity *[see Warnings and Precautions (5.7)]*

6.1 CLINICAL TRIALS EXPERIENCE

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety population from the randomized, double-blind, placebo-controlled clinical study included 720 patients with relapsed and/or refractory multiple myeloma, who received NINLARO in combination with lenalidomide and dexamethasone (NINLARO regimen; N=360) or placebo in combination with lenalidomide and dexamethasone (placebo regimen; N=360).

The most frequently reported adverse reactions (≥ 20%) in the NINLARO regimen and greater than the placebo regimen were diarrhea, constipation, thrombocytopenia, peripheral neuropathy, nausea, peripheral edema, vomiting, and back pain. Serious adverse reactions reported in ≥ 2% of patients included thrombocytopenia (2%) and diarrhea (2%). For each adverse reaction, one or more of the three drugs was discontinued in ≤ 1% of patients in the NINLARO regimen.

Table 4: Non-Hematologic Adverse Reactions Occurring in ≥ 5% of Patients with a ≥ 5% Difference Between the NINLARO Regimen and the Placebo Regimen (All Grades, Grade 3 and Grade 4)

	NINLARO + Lenalidomide and Dexamethasone N=360			Placebo + Lenalidomide and Dexamethasone N=360		
System Organ Class / Preferred Term	**N (%)**			**N (%)**		
	All	**Grade 3**	**Grade 4**	**All**	**Grade 3**	**Grade 4**
Infections and infestations						
Upper respiratory tract infection	69 (19)	1 (< 1)	0	52 (14)	2 (< 1)	0
Nervous system disorders						
Peripheral neuropathies*	100 (28)	7 (2)	0	77 (21)	7 (2)	0
Gastrointestinal disorders						
Diarrhea	151 (42)	22 (6)	0	130 (36)	8 (2)	0
Constipation	122 (34)	1 (< 1)	0	90 (25)	1 (< 1)	0
Nausea	92 (26)	6 (2)	0	74 (21)	0	0
Vomiting	79 (22)	4 (1)	0	38 (11)	2 (< 1)	0
Skin and subcutaneous tissue disorders						
Rash*	68 (19)	9 (3)	0	38 (11)	5 (1)	0
Musculoskeletal and connective tissue disorders						
Back pain	74 (21)	2 (< 1)	0	57 (16)	9 (3)	0
General disorders and administration site conditions						
Edema peripheral	91 (25)	8 (2)	0	66 (18)	4 (1)	0

Note: Adverse reactions included as preferred terms are based on MedDRA version 16.0.

*Represents a pooling of preferred terms

(Continued on next page)

Brief Summary (cont'd)

Table 5 represents pooled information from adverse event and laboratory data.

Table 5: Thrombocytopenia and Neutropenia

	NINLARO + Lenalidomide and Dexamethasone N=360		Placebo + Lenalidomide and Dexamethasone N=360	
	N (%)		N (%)	
	Any Grade	Grade 3-4	Any Grade	Grade 3-4
Thrombocytopenia	281 (78)	93 (26)	196 (54)	39 (11)
Neutropenia	240 (67)	93 (26)	239 (66)	107 (30)

Herpes Zoster

Herpes zoster was reported in 4% of patients in the NINLARO regimen and 2% of patients in the placebo regimen. Antiviral prophylaxis was allowed at the physician's discretion. Patients treated in the NINLARO regimen who received antiviral prophylaxis had a lower incidence (< 1%) of herpes zoster infection compared to patients who did not receive prophylaxis (6%).

Eye Disorders

Eye disorders were reported with many different preferred terms but in aggregate, the frequency was 26% in patients in the NINLARO regimen and 16% of patients in the placebo regimen. The most common adverse reactions were blurred vision (6% in the NINLARO regimen and 3% in the placebo regimen), dry eye (5% in the NINLARO regimen and 1% in the placebo regimen), and conjunctivitis (6% in the NINLARO regimen and 1% in the placebo regimen). Grade 3 adverse reactions were reported in 2% of patients in the NINLARO regimen and 1% in the placebo regimen.

Adverse Reactions Reported Outside of the Randomized Controlled Trial

The following serious adverse reactions have each been reported at a frequency of < 1%: acute febrile neutrophilic dermatosis (Sweet's syndrome), Stevens-Johnson syndrome, transverse myelitis, posterior reversible encephalopathy syndrome, tumor lysis syndrome, and thrombotic thrombocytopenic purpura.

7 DRUG INTERACTIONS

7.1 Strong CYP3A Inducers: Avoid concomitant administration of NINLARO with strong CYP3A inducers (such as rifampin, phenytoin, carbamazepine, and St. John's Wort).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy:

Risk Summary: Based on its mechanism of action and data from animal reproduction studies, NINLARO can cause fetal harm when administered to a pregnant woman. There are no human data available regarding the potential effect of NINLARO on pregnancy or development of the embryo or fetus. Ixazomib caused embryo-fetal toxicity in pregnant rats and rabbits at doses resulting in exposures that were slightly higher than those observed in patients receiving the recommended dose. Advise women of the potential risk to a fetus and to avoid becoming pregnant while being treated with NINLARO. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. *Animal Data*: In an embryo-fetal development study in pregnant rabbits there were increases in fetal skeletal variations/abnormalities (caudal vertebrae, number of lumbar vertebrae, and full supernumerary ribs) at doses that were also maternally toxic (≥ 0.3 mg/kg). Exposures in the rabbit at 0.3 mg/kg were 1.9 times the clinical time averaged exposures at the recommended dose of 4 mg. In a rat dose range-finding embryo-fetal development study, at doses that were maternally toxic, there were decreases in fetal weights, a trend towards decreased fetal viability, and increased post-implantation losses at 0.6 mg/kg. Exposures in rats at the dose of 0.6 mg/kg was 2.5 times the clinical time averaged exposures at the recommended dose of 4 mg.

8.2 Lactation: *Risk Summary*: No data are available regarding the presence of NINLARO or its metabolites in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Because the potential for serious adverse reactions from NINLARO in breastfed infants is unknown, advise nursing women not to breastfeed during treatment with NINLARO and for 90 days after the last dose.

8.3 Females and Males of Reproductive Potential: *Contraception*: Male and female patients of childbearing potential must use effective contraceptive measures during and for 90 days following treatment. Dexamethasone is known to be a weak to moderate inducer of CYP3A4 as well as other enzymes and transporters. Because NINLARO is administered with dexamethasone, the risk for reduced efficacy of contraceptives needs to be considered. Advise women using hormonal contraceptives to also use a barrier method of contraception.

8.4 Pediatric Use: Safety and effectiveness have not been established in pediatric patients.

8.5 Geriatric Use: Of the total number of subjects in clinical studies of NINLARO, 55% were 65 and over, while 17% were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Hepatic Impairment: In patients with moderate or severe hepatic impairment, the mean AUC increased by 20% when compared to patients with normal hepatic function. Reduce the starting dose of NINLARO in patients with moderate or severe hepatic impairment.

8.7 Renal Impairment: In patients with severe renal impairment or ESRD requiring dialysis, the mean AUC increased by 39% when compared to patients with normal renal function. Reduce the starting dose of NINLARO in patients with severe renal impairment or ESRD requiring dialysis. NINLARO is not dialyzable and therefore can be administered without regard to the timing of dialysis.

10 OVERDOSAGE: There is no known specific antidote for NINLARO overdose. In the event of an overdose, monitor the patient for adverse reactions and provide appropriate supportive care.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Dosing Instructions

- Instruct patients to take NINLARO exactly as prescribed.
- Advise patients to take NINLARO once a week on the same day and at approximately the same time for the first three weeks of a four week cycle.
- Advise patients to take NINLARO at least one hour before or at least two hours after food.
- Advise patients that NINLARO and dexamethasone should not be taken at the same time, because dexamethasone should be taken with food and NINLARO should not be taken with food.
- Advise patients to swallow the capsule whole with water. The capsule should not be crushed, chewed or opened.
- Advise patients that direct contact with the capsule contents should be avoided. In case of capsule breakage, avoid direct contact of capsule contents with the skin or eyes. If contact occurs with the skin, wash thoroughly with soap and water. If contact occurs with the eyes, flush thoroughly with water.
- If a patient misses a dose, advise them to take the missed dose as long as the next scheduled dose is ≥ 72 hours away. Advise patients not to take a missed dose if it is within 72 hours of their next scheduled dose.
- If a patient vomits after taking a dose, advise them not to repeat the dose but resume dosing at the time of the next scheduled dose.
- Advise patients to store capsules in original packaging, and not to remove the capsule from the packaging until just prior to taking NINLARO.

Thrombocytopenia: Advise patients that they may experience low platelet counts (thrombocytopenia). Signs of thrombocytopenia may include bleeding and easy bruising *[see Warnings and Precautions (5.1)]*.

Gastrointestinal Toxicities: Advise patients they may experience diarrhea, constipation, nausea and vomiting and to contact their physician if these adverse reactions persist *[see Warnings and Precautions (5.2)]*.

Peripheral Neuropathy: Advise patients to contact their physicians if they experience new or worsening symptoms of peripheral neuropathy such as tingling, numbness, pain, a burning feeling in the feet or hands, or weakness in the arms or legs *[see Warnings and Precautions (5.3)]*.

Peripheral Edema: Advise patients to contact their physicians if they experience unusual swelling of their extremities or weight gain due to swelling *[see Warnings and Precautions (5.4)]*.

Cutaneous Reactions: Advise patients to contact their physicians if they experience new or worsening rash *[see Warnings and Precautions (5.5)]*.

Thrombotic Microangiopathy: Advise patients to seek immediate medical attention if any signs or symptoms of thrombotic microangiopathy occur *[see Warnings and Precautions (5.6)]*.

Hepatotoxicity: Advise patients to contact their physicians if they experience jaundice or right upper quadrant abdominal pain *[see Warnings and Precautions (5.7)]*.

Other Adverse Reactions: Advise patients to contact their physicians if they experience signs and symptoms of acute febrile neutrophilic dermatosis (Sweet's syndrome), Stevens-Johnson syndrome, transverse myelitis, posterior reversible encephalopathy syndrome, tumor lysis syndrome, and thrombotic thrombocytopenic purpura *[see Adverse Reactions (6.1)]*.

Pregnancy: Advise women of the potential risk to a fetus and to avoid becoming pregnant while being treated with NINLARO and for 90 days following the final dose. Advise women using hormonal contraceptives to also use a barrier method of contraception. Advise patients to contact their physicians immediately if they or their female partner become pregnant during treatment or within 90 days of the final dose *[see Warnings and Precautions (5.8)]*.

Concomitant Medications: Advise patients to speak with their physicians about any other medication they are currently taking and before starting any new medications.

Please see full Prescribing Information for NINLARO at NINLAROhcp.com.

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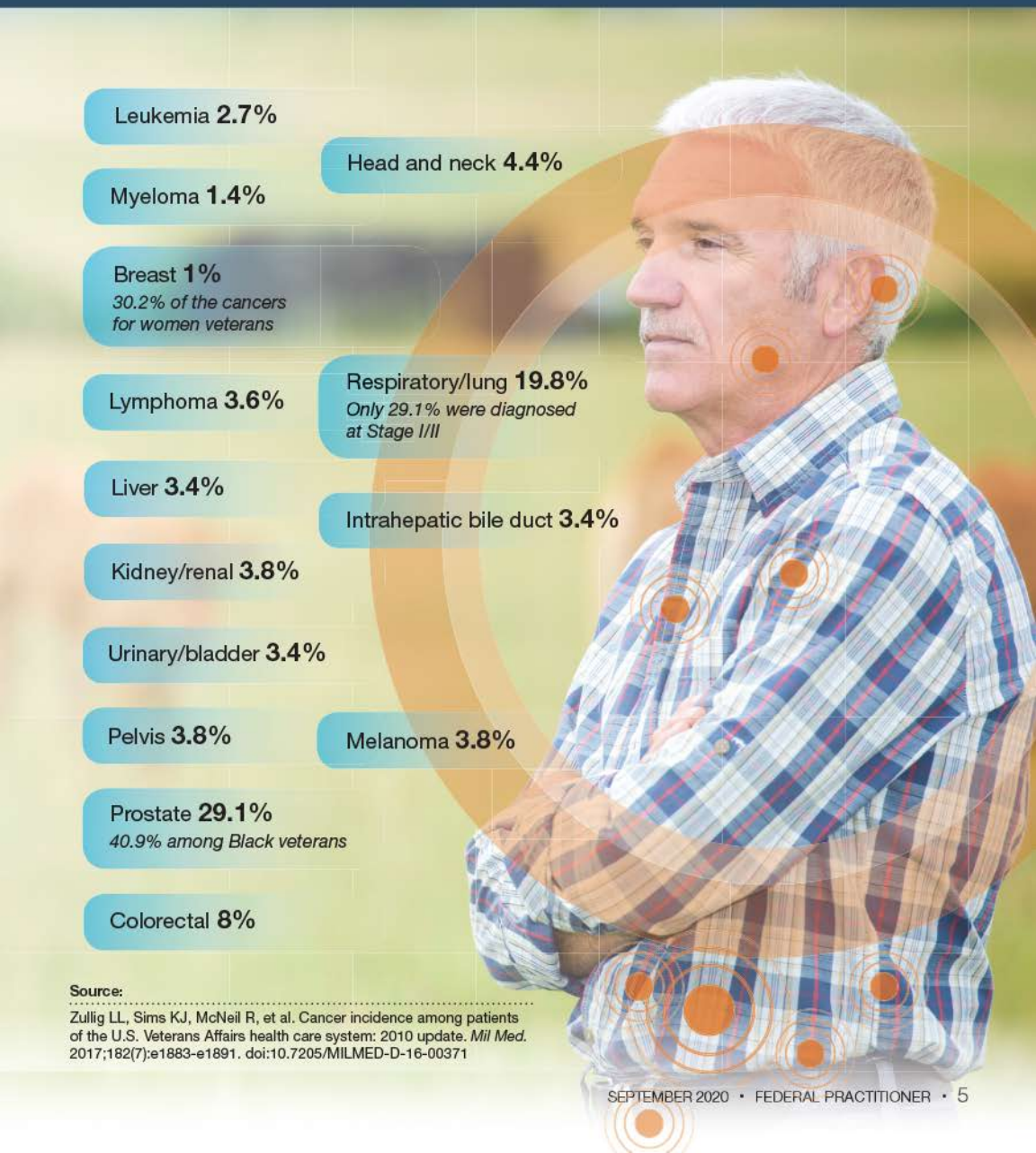
CANCER DATA TRENDS 2020

This issue was produced in collaboration with AVAHO

The Association of VA Hematology/Oncology (AVAHO), a nonprofit organization, provides a forum for interaction among VA hematology/oncology professionals across the nation. Its mission is to facilitate interaction and cooperation among VA hematology/oncology staff to enhance professional careers and improve patient care. AVAHO provides opportunities for networking, strengthening educational activities, and improving research capabilities among VA hematology/oncology professionals. Membership is extended to individuals interested in the organizational goals.

Cancer Incidence in the Veterans Health Administration

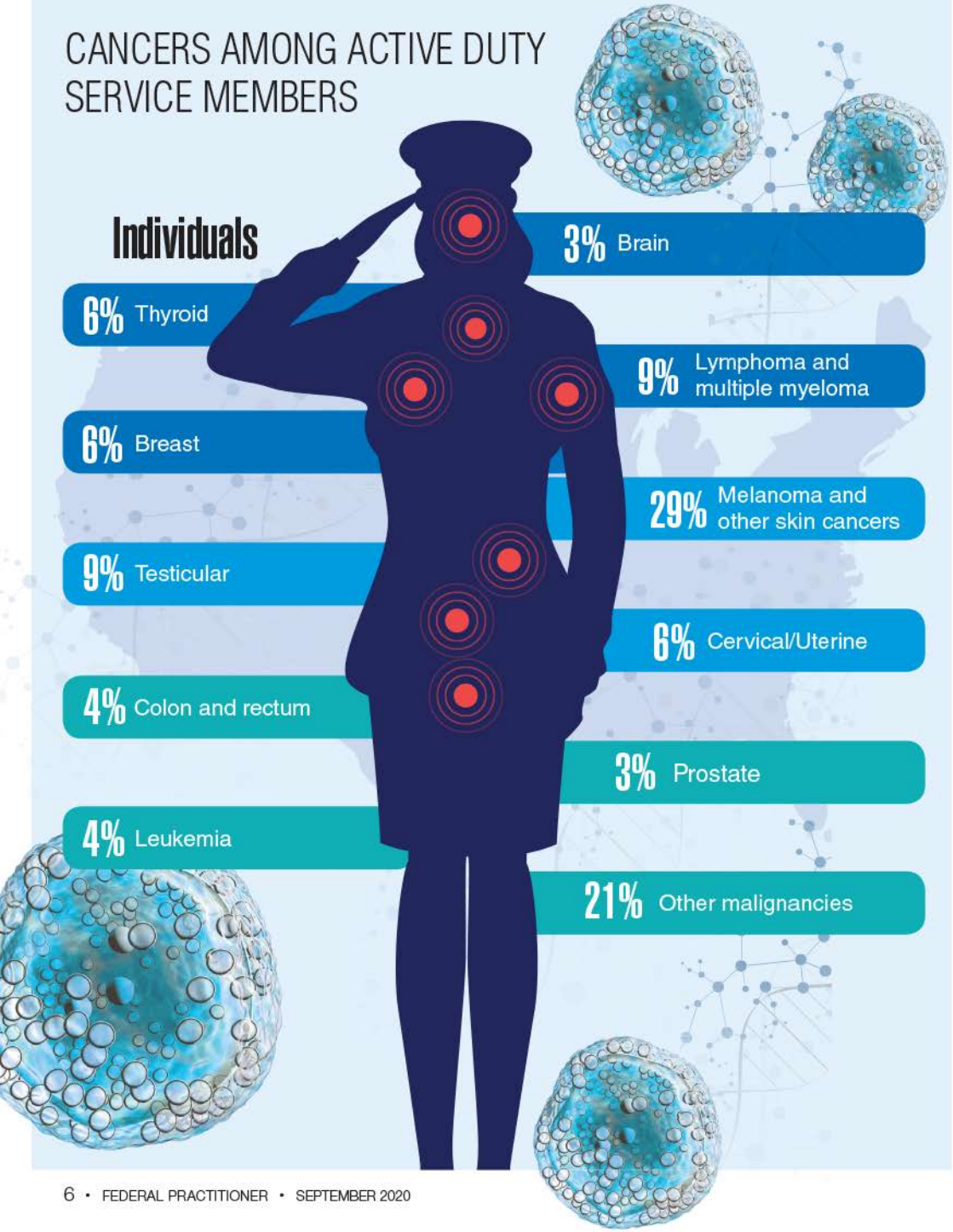
In the most recently available data (2010), 46,170 invasive cancers were diagnosed: 97% were diagnosed among men and 42% were among Southern veterans



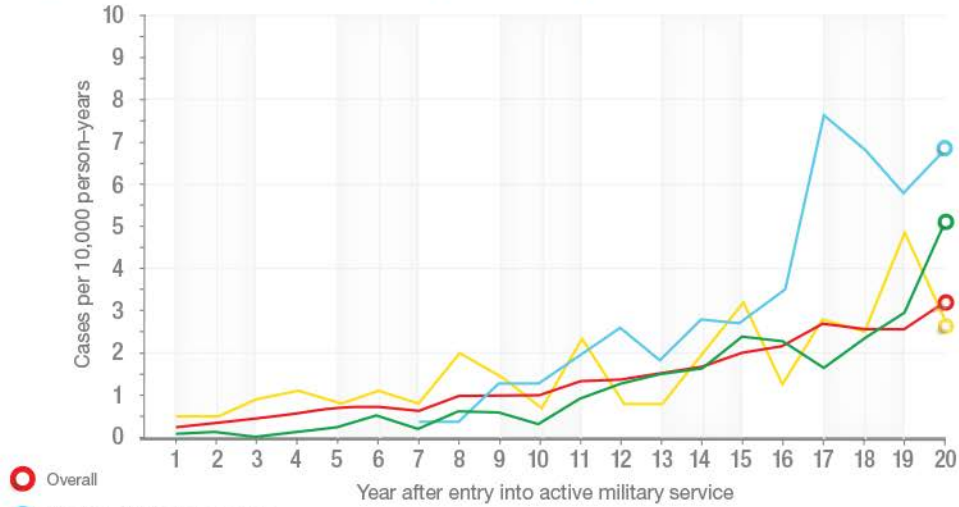
Source:

Zullig LL, Sims KJ, McNeil R, et al. Cancer incidence among patients of the U.S. Veterans Affairs health care system: 2010 update. *Mil Med.* 2017;182(7):e1883-e1891. doi:10.7205/MILMED-D-16-00371

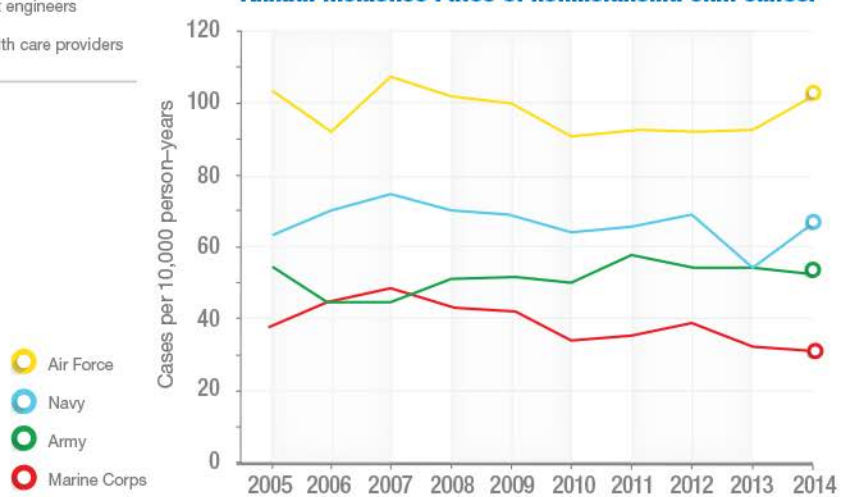
CANCERS AMONG ACTIVE DUTY SERVICE MEMBERS



Malignant melanoma incidence rates, by number of years of service



Annual incidence rates of nonmelanoma skin cancer



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Brundage JF, Williams VF, Stahlman S, McNellis MG. Incidence rates of malignant melanoma in relation to years of military service, overall and in selected military occupational groups, active component, U.S. Armed Forces, 2001–2015. *MSMR.* 2017;24(2):8-14.

CANCERS AMONG WOMEN

White Veterans

- 4% Thyroid/endocrine
- 30% Breast
- 17% Respiratory/lung
- 11% Gastrointestinal
- 3% Urinary/kidney
- 6% Uterine
- 2% Cervical
- 6% Melanoma
- 4% Lymphoma
- 2% Bone marrow
- 4% Central nervous system

Black Veterans

- 6% Thyroid/endocrine
- 31% Breast
- 11% Respiratory/lung
- 15% Gastrointestinal
- 7% Urinary/kidney
- 6% Uterine
- 3% Cervical
- 4% Lymphoma
- 5% Central nervous system

Breast Cancer Treatments in the Military Health System

In the Military Health System, beneficiaries can choose to receive care at Military Treatment Facilities (MTF), to purchase care from civilian care providers, or to use both

PURCHASED CARE – vs – MTF CARE

Women who used purchased care were **more likely to receive chemotherapy** (odds ratio [OR] 1.58) **and radiation** (OR 1.59) than women who received only MTF care

MTF CARE – vs – MTF + PURCHASED CARE

Women who utilized both types of care were **more likely to receive radiation** (OR 1.32) **and reconstructive surgery** (OR 1.30) than women who received only MTF care

Breast Cancer Stage at Diagnosis

Sources:

Manjelievskaia J, Brown D, Shao S, Hofmann K, Shriver CD, Zhu K. Breast cancer treatment and survival among Department of Defense beneficiaries: An analysis by benefit type and care source. *Mil Med.* 2018;183(3-4):e186-e195. doi:10.1093/milmed/usx031

Zullig LL, Goldstein KM, Sims KJ, et al. Cancer among women treated in the Veterans Affairs healthcare system. *J Womens Health (Larchmt).* 2019;28(2):268-275. doi:10.1089/jwh.2018.6936

EXPOSURE-RELATED CONDITIONS

Agent Orange Associated Conditions

***Bold* = cancer; *Italics* = proposed but not implemented**

Cancers of the larynx, trachea, and bronchus

Hodgkin and non-Hodgkin lymphoma and soft tissue sarcomas

Ischemic heart disease

Respiratory and lung cancers

Parkinson *(and Parkinson-like)* disease and peripheral neuropathy, early-onset

Porphyria cutanea tarda

Type 2 diabetes mellitus

Bladder cancer

Prostate cancer

Chronic B-cell leukemias

AL Amyloidosis

Multiple myeloma

Hypothyroidism

Chloracne or acneform disease

Camp Lejeune Contaminated Water Exposure Associated Conditions

***Bold* = cancer**

Adult leukemia

Myelodysplastic syndromes

Bladder cancer

Kidney cancer

Liver cancer

Multiple myeloma

Non-Hodgkin lymphoma

Parkinson disease

WARNING: Asbestos Exposure

Veterans who worked in mining, milling, shipyards, construction, carpentry, demolition or who worked with flooring, roofing, cement sheet, pipes, insulation, clutch facings, and brake linings **are at INCREASED risk of** mesothelioma and cancers of the lung, larynx, and ovary.

Source:

US Department of Veterans Affairs. Exposure to hazardous chemicals and materials. https://www.va.gov/disability/eligibility/hazardous-materials-exposure. Updated April 30, 2020. Accessed August 18, 2020.

SCREENING AND PREVENTION

Lung Cancer Screening Demonstration Project

In a demonstration project across **8 VA medical centers, >2,000 veterans** were screened for lung cancer with low dose computed tomography

60% HAD NODULES

56% HAD NODULES THAT REQUIRED TRACKING

2% **HAD NODULES THAT REQUIRED TRACKING AND FOLLOW-UP: CANCER FREE**

1.5% **HAD NODULES THAT REQUIRED TRACKING AND FOLLOW-UP: LUNG CANCER DIAGNOSED**

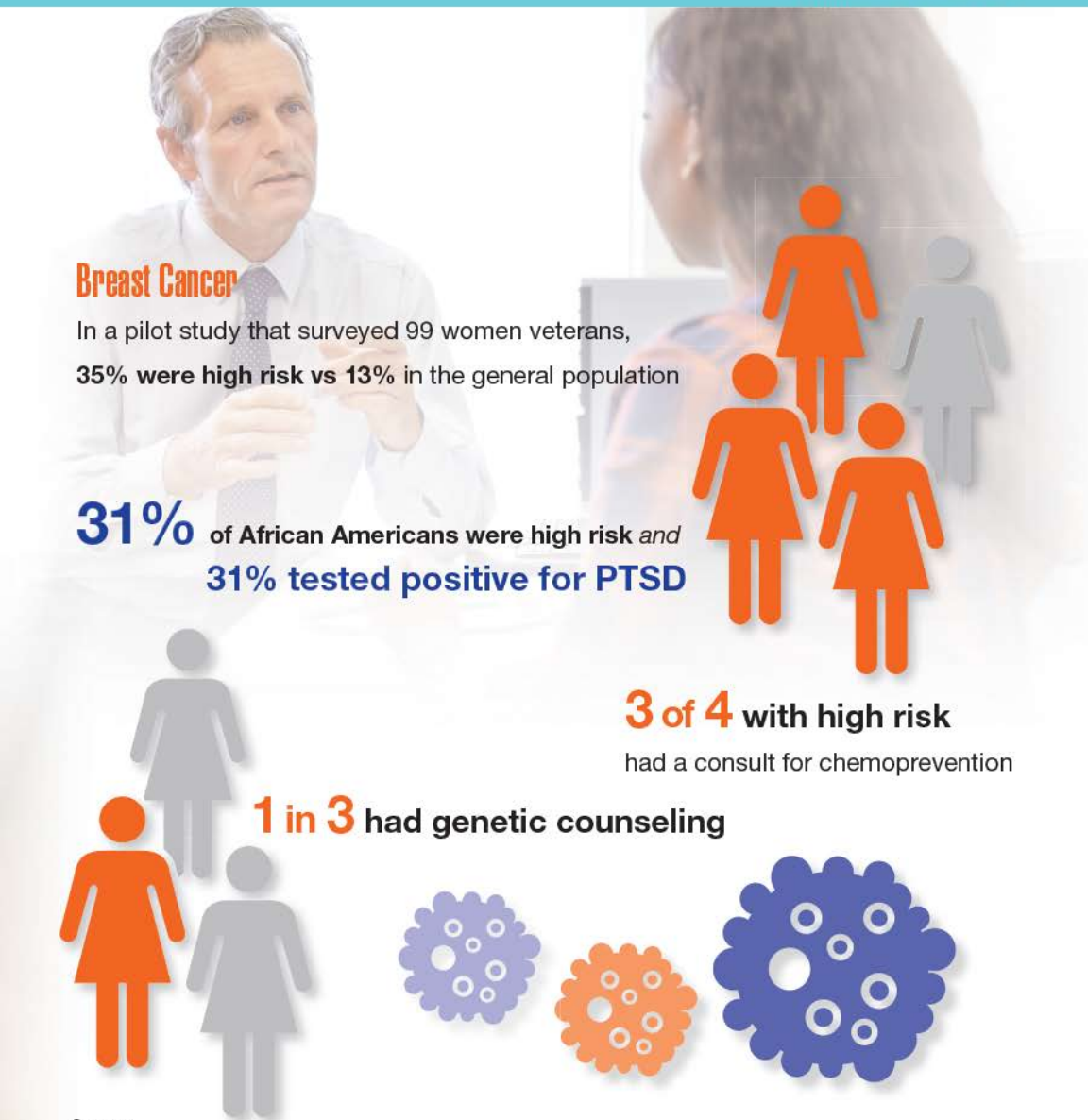
SCREENING AND PREVENTION

Colorectal Cancer

Screening rates were highest for patients who were mailed **fecal immunochemical tests (26.1%) vs usual care (5.8%)** or **screening invitation (7.7%)**

Hepatocellular Carcinoma

Nearly 50% of veterans with cirrhosis have **delays in diagnosis** of hepatocellular carcinoma of **60 days or more** after a **red flag** had been identified, defined by guidelines



Breast Cancer

In a pilot study that surveyed 99 women veterans,

35% were high risk vs 13% in the general population

31% **of African Americans were high risk** *and*

31% tested positive for PTSD

3 of 4 with high risk

had a consult for chemoprevention

1 in 3 had genetic counseling

Sources:

Goldshore MA, Mehta SJ, Fletcher W, Tzanis G, Doubeni CA, Paulson EC. An RCT of fecal immunochemical test colorectal cancer screening in veterans without recent primary care. *Am J Prev Med*. 2020;59(1):41-48. doi:10.1016/j.amepre.2020.02.014

Kinsinger LS, Anderson C, Kim J, et al. Implementation of lung cancer screening in the Veterans Health Administration. *JAMA Intern Med*. 2017;177(3):399-406. doi:10.1001/jamainternmed.2016.9022

Choi DT, Davila JA, Sansgiry S, et al. Factors associated with delay of diagnosis of hepatocellular carcinoma in patients with cirrhosis [published online ahead of print, 2020 Jul 18]. *Clin Gastroenterol Hepatol*. 2020;S1542-3565(20)30988-5. doi:10.1016/j.cgh.2020.07.026

Park Y-HA, Keller AT, Hsu T-CM, et al. Results of a high risk for breast cancer screening pilot in female veterans. In press

VA ONCOLOGY CENTERS OF EXCELLENCE

PROSTATE CANCER FOUNDATION-VA CENTERS OF EXCELLENCE
Funded Precision Oncology Center (POC) sites

ANN ARBOR, MI
Stewart J. Rahr Foundation POC

BOSTON, MA
Blaventik Family Foundation POC

BRONX. NY
Blavatnik Family Foundation POC

CHICAGO, IL
Robert Frederick Smith POC

DURHAM. NC
Michael and Lori Milken Family Foundation POC

LOS ANGELES, CA
David Geffen Foundation POC

MANHATTAN, NY
John and Daria Barry Foundation POC

PHILADELPHIA, PA
Jonathan and Plum Simons POC

SEATTLE, WA
Stephen J. Cloobeck POC

TAMPA AND BAY PINES, FL
John and Daria Barry Foundation POC

WASHINGTON, DC
Edward P. Evans Foundation POC

PROSTATE CANCER FOUNDATION-VA CENTERS OF EXCELLENCE
Other POC sites

BALTIMORE, MD
Greenebaum Comprehensive Cancer Center and Sidney Kimmel Cancer Center

DALLAS, TX
Harold C. Simmons Comprehensive Cancer Center

DENVER, CO
The University of Colorado

HOUSTON , TX
Dan L. Duncan Comprehensive Cancer Center and MD Anderson Cancer Center

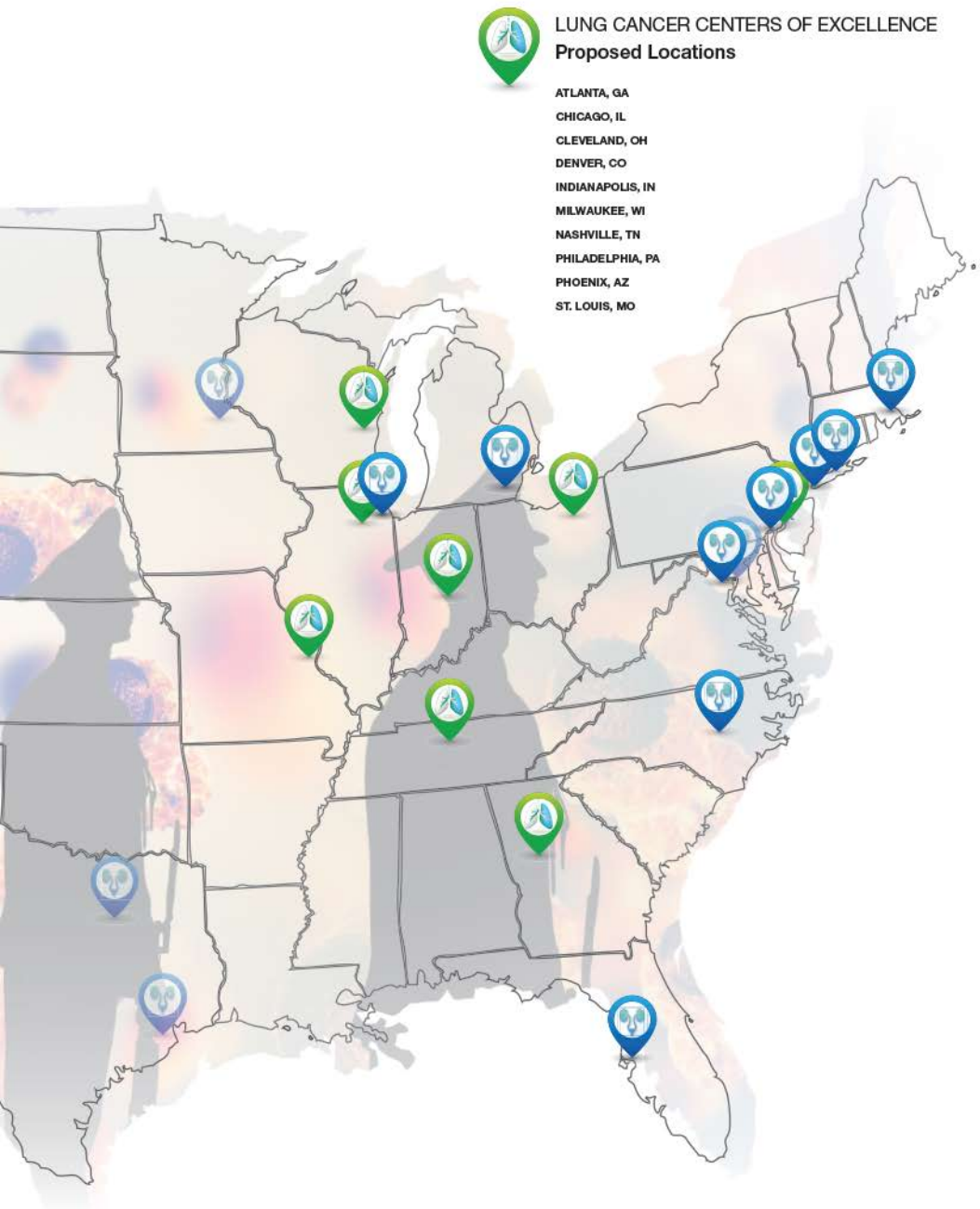
MINNEAPOLIS, MN
Masonic Cancer Center

PHOENIX, AZ
The University of Arizona Cancer Center

PORTLAND, OR
Knight Cancer Institute

SALT LAKE CITY, UT
Huntsman Cancer Institute

SAN FRANCISCO. CA
Diller Family Comprehensive Cancer Center


LUNG CANCER CENTERS OF EXCELLENCE
Proposed Locations
ATLANTA, GA
CHICAGO, IL
CLEVELAND, OH
DENVER, CO
INDIANAPOLIS, IN
MILWAUKEE, WI
NASHVILLE, TN
PHILADELPHIA, PA
PHOENIX, AZ
ST. LOUIS, MO

DISPARITIES IN CANCER CARE

The quality and efficacy of cancer care varies significantly for certain at risk populations that face elevated mortality risk

ALL CANCERS MORTALITY PROPORTION (per 100,000 age- and sex- standardized veterans)

Prostate Cancer Mortality Risk for Black Men

A study comparing the absolute difference in risk of prostate cancer-specific mortality 10 years after diagnosis found that compared with White men the risk for Black men in the US, Black veterans, and Black clinical trial participants was:

0.5% ↑ UNITED STATES

1.2% ↓ VETERANS*

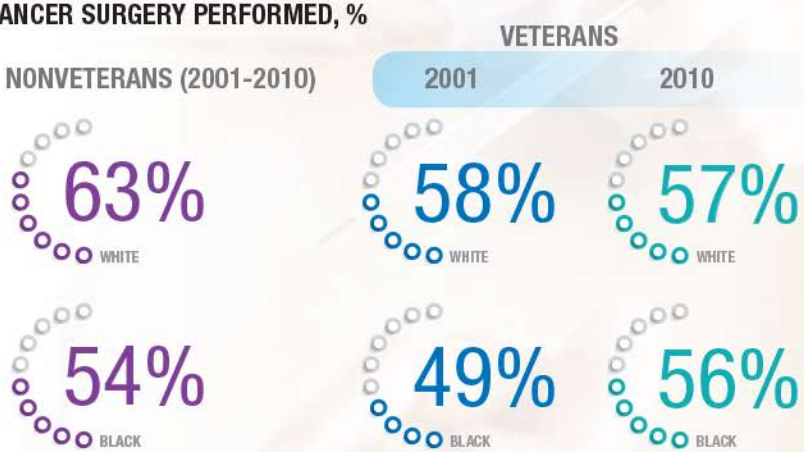
5.1% ↓ CLINICAL TRIAL PARTICIPANTS

* The difference between Black and White veterans was not statistically significant

Lung Cancer

In the US, Black patients experienced worse overall survival when compared with non-Hispanic White and Asian patients. One of the contributing causes is lower rates of surgery for Black patients.

LUNG CANCER SURGERY PERFORMED, %



In the study, **Black veterans** with surgery or other/no treatment **had better overall survival** than did White veterans

Gastric Cancer

SUBHAZARD RATIO OF INCIDENCE WHEN COMPARED WITH WHITE VETERANS

WHITE MEN:

BLACK MEN	ASIAN MEN	HISPANIC MEN	ALL WOMEN
2.00	2.52	1.59	0.52

Sources:

Dess RT, Hartman HE, Mahal BA, et al. Association of Black race with prostate cancer-specific and other-cause mortality. *JAMA Oncol.* 2019;5(7):975-983. doi:10.1001/jamaoncol.2019.0826

Kumar S, Metz DC, Ellenberg S, Kaplan DE, Goldberg DS. Risk factors and incidence of gastric cancer after detection of Helicobacter pylori infection: a large cohort study. *Gastroenterology.* 2020;158(3):527-536.e7. doi:10.1053/j.gastro.2019.10.019

Lynch KE, Viernes B, Khader K, DuVall SL, Schroeck FR. Sex and the diagnostic pathway to bladder cancer among veterans: no evidence of disparity. *Womens Health Issues.* 2020;30(2):128-135. doi:10.1016/j.whi.2019.11.001

Soneji S, Tanner NT, Silvestri GA, Lathan CS, Black W. Racial and ethnic disparities in early-stage lung cancer survival. *Chest.* 2017;152(3):587-597. doi:10.1016/j.chest.2017.03.059

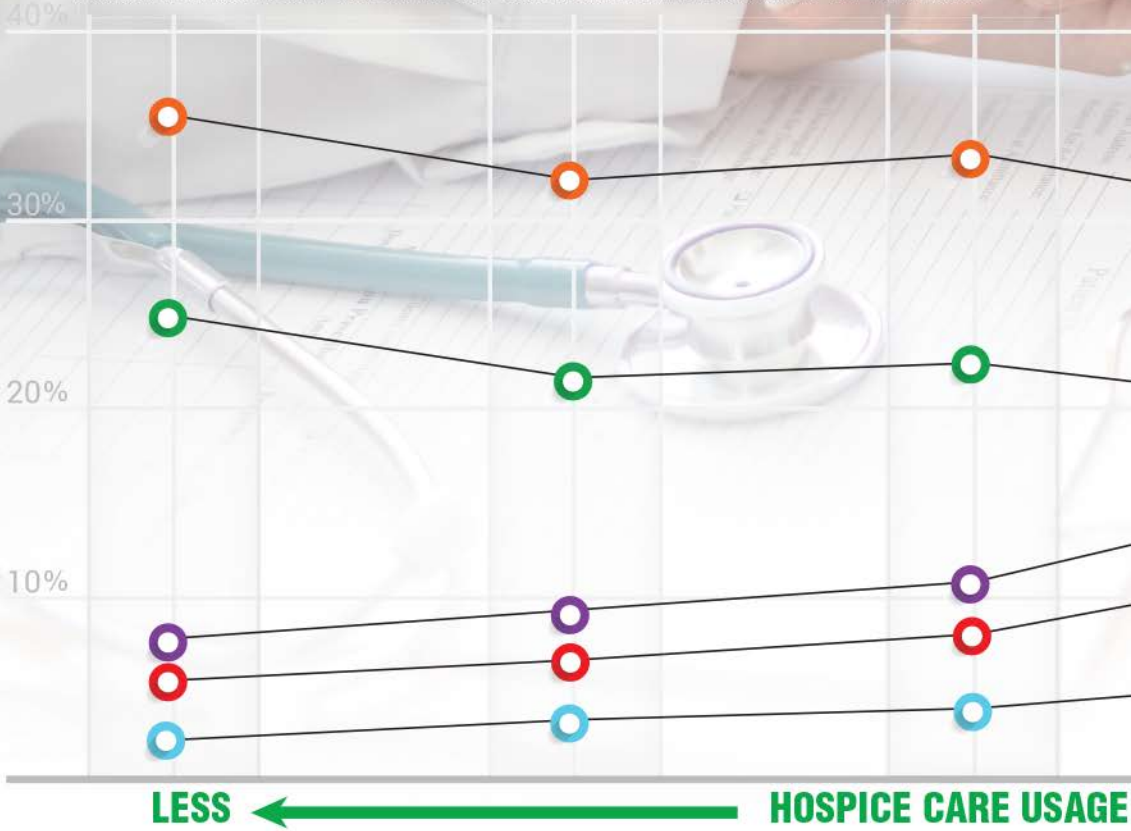
Williams CD, Salama JK, Moghanaki D, Karas TZ, Kelley MJ. Impact of race on treatment and survival among U.S. veterans with early-stage lung cancer. *J Thorac Oncol.* 2016;11(10):1672-1681. doi:10.1016/j.jtho.2016.05.030

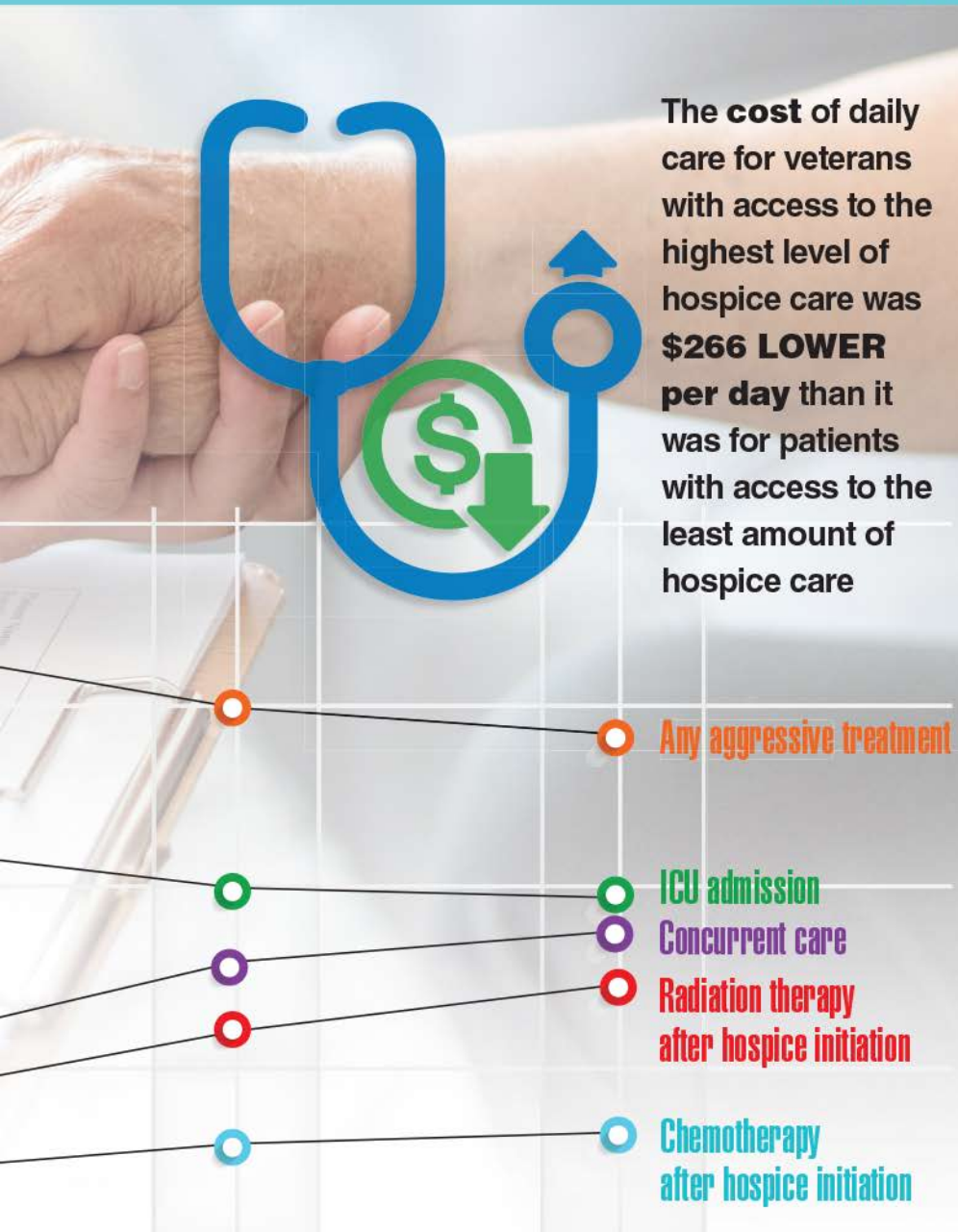
Wong MS, Hoggatt KJ, Steers WN, et al. Racial/ethnic disparities in mortality across the Veterans Health Administration. *Health Equity.* 2019;3(1):99-108. doi:10.1089/heq.2018.0086

HOSPICE CARE

VA Comprehensive End-of-Life Care Initiative is an innovative program that allows veterans to continue to receive both treatment and hospice care. A recent study by VA researchers examined the impact of the both/and approach for veterans with advanced lung cancer and found that access to hospice care without restricting treatment was associated with less aggressive medical treatment and significantly lower medical costs.

THE BETTER THE HOSPICE CARE, THE MORE LIKELY VETERANS WERE TO USE IT AND THE LESS LIKELY THEY ARE TO USE **AGGRESSIVE** CANCER TREATMENTS





Source:

Mor V, Wagner TH, Levy C, et al. Association of expanded VA hospice care with aggressive care and cost for veterans with advanced lung cancer. *JAMA Oncol.* 2019;5(6):810-816. doi:10.1001/jamaoncol.2019.0081

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