ORIGINAL RESEARCH

Reducing Sex Disparities in Statin Therapy Among Female Veterans With Type 2 Diabetes and/or Cardiovascular Disease

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Background: Female veterans have higher rates of cardiovascular disease (CVD) compared with the civilian population. Medical management with statins (3-hydroxy-3-methyl-glutaryl-coenzmye A reductase inhibitors) is the cornerstone of lipid-lowering therapy and cardiovascular risk reduction. Despite eligibility, female veterans are less likely to receive statin therapy than their male counterparts. This project aimed to increase statin prescribing for female veterans with type 2 diabetes mellitus (T2DM) and CVD to reduce sex disparities.

Methods: The primary objective of this project was to increase statin prescribing among female veterans with T2DM and/or CVD to reduce cardiovascular risk. Secondary outcomes included increased pharmacogenomic testing and the assessment of pharmacogenomic results related to statin therapy. The Primary Care Equity Dashboard (PCED) was used to identify female veterans without a statin prescription. A clinical pharmacist practitioner (CPP) contacted those identified to offer statin therapy and pharmacogenomic testing.

Results: Of the 129 contacted veterans, 31 (24.0%) had a non-US Department of Veterans Affairs (VA) statin prescription, 13 (10.1%) had an active VA statin prescription and 85 (65.9%) did not have a statin prescription despite their eligibility. Of the 85 veterans with no active statin therapy, 37 (43.5%) were initiated on a statin. The percentage of female veterans with an active statin prescription increased from 77.8% to 79.0% for those with T2DM and from 82.2% to 90.2% for those with CVD. Seventy-one veterans agreed to pharmacogenomic testing, and 47 completed testing. Five patients had abnormal results that may impact statin tolerability.

Conclusions: The percentage of female veterans with T2DM and/or CVD with a statin prescription increased following CPP outreach. Pharmacogenomic testing should be used for statin prescribing and adherence.

Cardiovascular disease (CVD) is the leading cause of death among women in the United States.[1] Most CVD is due to the buildup of plaque (ie, cholesterol, proteins, calcium, and inflammatory cells) in artery walls.[2] The plaque may lead to atherosclerotic cardiovascular disease (ASCVD), which includes coronary heart disease, cerebrovascular disease, peripheral artery disease, and aortic atherosclerotic disease.[2,3] Control and reduction of ASCVD risk factors, including high cholesterol levels, elevated blood pressure, insulin resistance, smoking, and a sedentary lifestyle, can contribute to a reduction in ASCVD morbidity and mortality.[2] People with type 2 diabetes mellitus (T2DM) have an increased prevalence of lipid abnormalities, contributing to their high risk of ASCVD.[4,5]

The prescribing of statins (3-hydroxy-3-methyl-glutaryl-coenzmye A reductase inhibitors) is the cornerstone of lipid-lowering therapy and cardiovascular risk reduction for primary and secondary prevention of ASCVD.[6] The American Diabetes Association (ADA) and American College of Cardiology/American Heart Association (ACC/AHA) recommend moderate- to high-intensity statins for primary prevention in patients with T2DM and high-intensity statins for secondary prevention in those with or without diabetes when not contraindicated.[4,5,7] Despite eligibility according to guideline recommendations, research predominantly shows that women are less likely to receive statin therapy; however, this trend is improving.[6,8-11] To explain the sex differences in statin use, Nanna et al found that there is a combination of women being offered statin therapy less frequently, declining therapy more frequently, and discontinuing treatment more frequently.[11] One possibility for discontinuing treatment could be statin-associated muscle symptoms (SAMS), which occur in about 10% of patients.[12] The incidence of adverse effects (AEs) may be related to the way statins are metabolized.

Pharmacogenomic testing is free for veterans through the US Department of Veterans Affairs (VA) PHASER program, which offers information and recommendations for a panel of 11 gene variants. The panel includes genes related to common medication classes such as anticoagulants, antiplatelets, proton pump inhibitors, nonsteroidal anti-inflammatory drugs, opioids, antidepressants, and statins. The VA PHASER panel includes the solute carrier organic anion transporter family member 1B1 (*SLCO1B1*) gene, which is predominantly expressed in the liver and facilitates the hepatic uptake of most statins.[13,14] A reduced function of *SLCO1B1* can lead to higher statin levels, resulting

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TABLE 1. Baseline Patient Demographics (N = 129)

Criteria	Results
Age, mean, y	59
Race, No. (%)	
Black	107 (82.9)
White	17 (13.2)
Asian	1 (0.8)
Unknown/other	4 (3.1)
Confirmed diagnosis, No. (%)	
Type 2 diabetes mellitus	116 (89.9)
Cardiovascular disease	4 (3.1)
Both	9 (7.0)

TABLE 2. Reasons for Declining Statin Therapy (n = 48)

Reason	No. (%)
Concern for adverse effects	17 (35)
Unknown/other	12 (25)
Pill burden	5 (10)
Wanted to consult with primary care physician	5 (10)
Prefer lifestyle modifications/natural remedies	5 (10)
Does not currently see value in statins	4 (8)

in increased concentrations that may potentially cause SAMS.[13,14] Some alleles associated with reduced function include *SLCO1B1*5*, **15*, **23*, **31*, and **46* to **49*, whereas others are associated with increased function, such as *SLCO1B1 *14* and **20* (Appendix).[15] Supporting evidence shows the *SLCO1B1*5* nucleotide polymorphism increases plasma levels of simvastatin and atorvastatin, affecting effectiveness or toxicity.[13] Females tend to have a lower body weight and higher percentage of body fat compared with males, which might lead to higher concentrations of lipophilic drugs, including atorvastatin and simvastatin, which may be exacerbated by decreased function of *SLCO1B1*5*.[15] With pharmacogenomic testing, therapeutic recommendations can be made to improve the overall safety and efficacy of statins, thus improving adherence using a patient-specific approach.[14,15]

METHODS

Carl Vinson VA Medical Center (CVVAMC) serves about 42,000 veterans in Central and South Georgia, of which about 15% are female. Of the female veterans enrolled in care, 63% identify as Black, 27% White, and 1.5% as Asian, American Indian/Alaska Native, or Native Hawaiian/Other Pacific Islander. The 2020 Veterans Chartbook report showed that female veterans and minority racial and ethnic groups had worse access to health care and higher mortality rates than their male and non-Hispanic White counterparts.[16]

The Primary Care Equity Dashboard (PCED) was developed to engage the VA health care workforce in the process of identifying and addressing inequities in local patient populations.[17] Using electronic quality measure data, the PCED provides Veterans Integrated Service Network-level and facility-level performance on several metrics.[18] The PCED had not been previously used at the CVVAMC, and few publications or quality improvement projects regarding its use have been reported by the VA Office of Health Equity. PCED helped identify disparities when comparing female to male patients in the prescribing of statin therapy for patients with CVD and statin therapy for patients with T2DM.

VA PHASER pharmacogenomic analyses provided an opportunity to expand this quality improvement project. Sanford Health and the VA collaborated on the PHASER program to offer free genetic testing for veterans. The program launched in 2019 and expanded to various VA sites, including CVVAMC in March 2023. This program has been extended to December 31, 2025.

The primary objective of this quality improvement project was to increase statin prescribing among female veterans with T2DM and/or CVD to reduce cardiovascular risk. Secondary outcomes included increased pharmacogenomic testing and the assessment of pharmacogenomic results related to statin therapy. This project was approved by the CVVAMC Pharmacy and Therapeutics Committee. The PCED was used to identify female veterans with T2DM and/or CVD without an active prescription for a statin between July and October 2023. A review of Computerized Patient Record System patient charts was completed to screen for prespecified inclusion and exclusion criteria. Veterans were included if they were assigned female at birth, were enrolled in care at CVVAMC, and had a diagnosis of T2DM or CVD (history of myocardial infarction, coronary bypass graft, percutaneous coronary intervention, or other revascularization in any setting).

Veterans were excluded if they were currently pregnant, trying to conceive, breastfeeding, had a T1DM diagnosis, had previously documented hypersensitivity to a statin, active liver failure or decompensated cirrhosis, previously documented statin-associated rhabdomyolysis or autoimmune myopathy, an active prescription for a proprotein convertase subtilisin/kexin type

9 inhibitor, or previously documented statin intolerance (defined as the inability to tolerate ≥ 3 statins, with ≥ 1 prescribed at low intensity or alternate-day dosing). The female veterans were compared to 2 comparators: the facility's male veterans and the VA national average, identified via the PCED.

Once a veteran was screened, they were telephoned between October 2023 and February 2024 and provided education on statin use and pharmacogenomic testing using a standardized note template. An order was placed for participants who provided verbal consent for pharmacogenomic testing. Those who agreed to statin initiation were referred to a clinical pharmacist practitioner (CPP) who contacted them at a later date to prescribe a statin following the recommendations of the 2019 ACC/AHA and 2023 ADA guidelines and pharmacogenomic testing, if applicable.[4,5,7] Appropriate monitoring and follow-up occurred at the discretion of each CPP. Data collection included: age, race, diagnoses (T2DM, CVD, or both), baseline lipid panel (total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein), hepatic function, name and dose of statin, reasons for declining statin therapy, and pharmacogenomic testing results related to *SLCO1B1*.

RESULTS

At baseline in July 2023, 77.8% of female veterans with T2DM were prescribed a statin, which exceeded the national VA average (77.0%), but was below the rate for male veterans (78.7%) in the facility comparator group.[17] Additionally, 82.2% of females with CVD were prescribed a statin, which was below the national VA average of 86.0% and the 84.9% of male veterans in the facility comparator group.[17] The PCED identified 189 female veterans from July 2023 to October 2023 who may benefit from statin therapy. Thirty-three females met the exclusion criteria. Of the 156 included veterans, 129 (82.7%) were successfully contacted and 27 (17.3%) could not be reached by telephone after 3 attempts (Figure 1). The 129 female veterans contacted had a mean age of 59 years and the majority were Black (82.9%) (Table 1).

Primary Outcomes

Of the 129 contacted veterans, 31 (24.0%) had a non-VA statin prescription, 13 (10.1%) had an active VA statin prescription, and 85 (65.9%) did not have a statin prescription, despite being eligible. Statin adherence was confirmed with participants, and the medication list was updated accordingly.

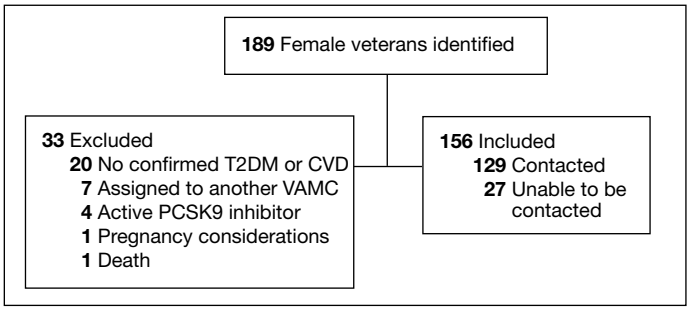

FIGURE 1. Flow Diagram of Patient Selection

Abbreviations: CVD, cardiovascular disease; PCSK9, proprotein convertase subtilisin/kexin type 9; T2DM, type 2 diabetes mellitus; VAMC, Veterans Affairs medical center.

Of the 85 veterans with no active statin therapy, 37 (43.5%) accepted a new statin prescription and 48 (56.5%) declined. There were various reasons provided for declining statin therapy: 17 participants (35.4%) declined due to concern for AEs (Table 2).

From July 2023 to March 2024, the percentage of female veterans with active statin therapy with T2DM increased from 77.8% to 79.0%. For those with active statin therapy with CVD, usage increased from 82.2% to 90.2%, which exceeded the national VA average and facility male comparator group (Figures 2 and 3).[17]

Secondary Outcomes

Seventy-one of 129 veterans (55.0%) gave verbal consent, and 47 (66.2%) completed the pharmacogenomic testing; 58 (45.0%) declined. Five veterans (10.6%) had a known *SLCO1B1* allele variant present. One veteran required a change in statin therapy based on the results (eAppendix, available at doi:10.12788/fp.0624).

DISCUSSION

This project aimed to increase statin prescribing among female veterans with T2DM and/or CVD to reduce cardiovascular risk and increase pharmacogenomic testing using the PCED and care managed by CPPs. The results of this quality improvement project illustrated that both metrics have improved at CVVAMC as a result of the intervention. The results in both metrics now exceed the PCED national VA average, and the CVD metric also exceeds that of the facility male comparator group. While there was only a 1.2% increase from July 2023 to March 2024 for patients with T2DM, there was an 8.0% increase for patients with CVD. Despite standardized education on statin use, more veterans declined therapy than accepted it, mostly due to concern for AEs. Recording the reasons for declining statin therapy offered

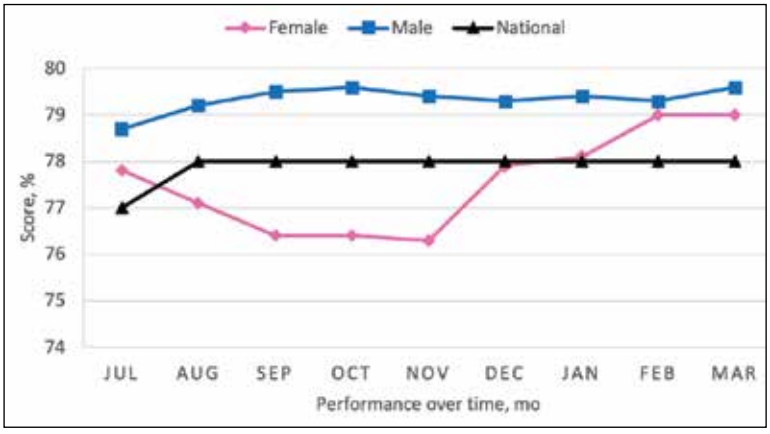

FIGURE 2. Statin Prescribing in Veterans With Type 2 Diabetes Mellitus

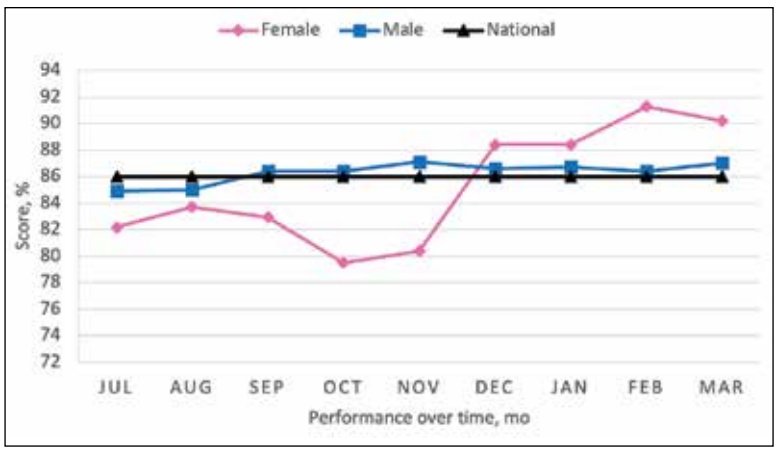

FIGURE 3. Statin Prescribing in Veterans With Cardiovascular Disease

valuable insight that can be used in additional discussions with veterans and clinicians.

Pharmacogenomics gives clinicians the unique opportunity to take a proactive approach to better predict drug responses, potentially allowing for less trial and error with medications, fewer AEs, greater trust in the clinician, and improved medication adherence. The CPPs incorporated pharmacogenomic testing into their practice, which led to identifying 5 *SLCO1B1* gene abnormalities. The PCED served as a powerful tool for advancing equity-focused quality improvement initiatives on a local level and was crucial in prioritizing the detection of veterans potentially receiving suboptimal care.

Limitations

The nature of "cold calls" made it challenging to establish contact for inclusion in this study. An alternative to increase engagement could have been scheduled phone or face-to-face visits. While the use of the PCED was crucial, data did not account for statins listed in the non-VA medication list. All 31 patients with statins prescribed outside the VA had a start date added to provide the most accurate representation of the data moving forward.

Another limitation in this project was its small sample size and population. CVVAMC serves about 6200 female veterans, with roughly 63% identifying as Black. The preponderance of Black individuals (83%) in this project is typical for the female patient population at CVVAMC but may not reflect the demographics of other populations. Other limitations to this project consisted of scheduling conflicts. Appointments for laboratory draws at community-based outpatient clinics were subject to availability, which resulted in some delay in completion of pharmacogenomic testing.

CONCLUSIONS

CPPs can help reduce inequity in health care delivery. Increased incorporation of the PCED into regular practice within the VA is recommended to continue addressing sex disparities in statin use, diabetes control, blood pressure management, cancer screenings, and vaccination needs. CVVAMC plans to expand its use through another quality improvement project focused on reducing sex disparities in blood pressure management. Improving educational resources made available to veterans on the importance of statin therapy and potential to mitigate AEs through use of the VA PHASER program also would be helpful. This project successfully improved CVVAMC metrics for female veterans appropriately prescribed statin therapy and increased access to pharmacogenomic testing. Most importantly, it helped close the sex-based gap in CVD risk reduction care.

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Ethics and consent

This study was exempt from institutional review board review and approved by the CVVAMC Pharmacy and Therapeutic Committee.

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APPENDIX. Pharmacogenomic Results and Therapy Considerations

Patient	Allele variant	Clinical relevance	Statin status	Outcome
1	**15*	Decreased function[a]	Rosuvastatin 20 mg daily (high intensity)	Veterans pharmacogenomic results show an allele variation associated with decreased function. The statin was prescribed by community-based prescriber and veteran reported no intolerance. Veterans tolerance was likely due to less than maximum dosage with pharmacogenomic implications based on phenotype.
2	**15*	Decreased function[a]	Rosuvastatin 10 mg daily (moderate intensity)	Veterans pharmacogenomic results show an allele variation associated with decreased function. Veteran reported no intolerance. Veterans tolerance was likely due to less than maximum dosage with pharmacogenomic implications based on phenotype.
3	**5* and **15*	Poor function[a]	Rosuvastatin 10 mg daily (moderate intensity)	Veterans pharmacogenomic results show an allele variation associated with decreased function. Veteran was unable to tolerate rosuvastatin 10 mg daily thus changed to pravastatin 40 mg daily.
4	**5* and **15*	Poor function[a]	No statin	Veterans pharmacogenomic results show an allele variation associated with poor function. However, veteran was not currently on statin treatment at the time of results due to follow up with clincial pharmacist practitoner pending.
5	**14*	Increased function	Atorvastatin 20 mg daily (moderate intensity)	Veterans pharmacogenomic results show an allele variation associated with increased function. Veteran reported no intolerance to atorvastatin 20 mg daily. Increased function on **14* shows a normal/routine/low-risk priority to change therapy thus therapy remained the same.

[a]A genetic variation associated with decreased or poor function results in diminished hepatocellular uptake which limits hepatic clearance thus leading to increased risk of adverse effects.

eAPPENDIX. List of Mutated Genes and Specific Mutations With Respective Frequency in the Study Population (N = 35)

Gene	Mutation	Mutation, No. (%)
TERT promoter	c.-146C>T	18 (51)
	c.-124C>T	8 (23)
	139_-138CC>TT	1 (3)
	Total	27 (77)
CDKN2A/B	Loss both	2 (6)
	Copy number loss both	2 (6)
	p.P81L missense LOF 35.7%	1 (3)
	P16INK4a splice site 151-1_151GG>AA and p14ARF splice site 194-1_194GG>AA subclonal	1 (3)
	p16INK4a P70fs*36 and p14ARF Q85fs*62	1 (3)
	p16INK4a F90L and p14ARF P105T	1 (3)
	CDKN2A p.V51I splice region variant LOF 76.3%	1 (3)
	p16INK4a R80* and p14ARF P94L, p16INK4a P81L	1 (3)
	CDKN2A p.A57fs frameshift LOF 33.2%	1 (3)
	CDKN2A p.W110* stop gain LOF 8.7%	1 (3)
	Loss unspecified	1 (3)
	CDKN2A loss	1 (3)
	p16INK4a splice site 151-25_188del63 and p14ARF splice site 194-25_231del63	1 (3)
	Total	15 (43)
BRAF	V600E	7 (20)
	V600K	6 (17)
	Total	13 (37)
NF1	Loss exons 1-7	1 (3)
	p.R1241 stop gain LOF 60.2%	1 (3)
	p.Q1815* stop gain LOF 32.8%	1 (3)
	1527+1_1527+2GT>TC splice site	1 (3)
	p.Q1822* stop gain LOF 49.8%	1 (3)
	Q1395*, Q519* splice site 6007-1G>A	1 (3)
	Q1617*, rearrangement intron 1	1 (3)
	R1204W, W1685*	1 (3)
	p.Q589* stop gain LOF 65.6%	1 (3)
	p.Q1255* stop gain LOF 14.5% p.R2450* stop gain LOF 11.7%	1 (3)
	Q519*, Y2192*	1 (3)
	Total	11 (31)
TP53	p.IR195 stop gain LOF 40.5%	1 (3)
	p.P27L missense LOF 14.9%	1 (3)
	c.559+1G>T splice region variant LOF 38.4%	1 (3)
	p.R110fs frameshift LOF 51.7%	1 (3)
	R213*	1 (3)
	R282W	1 (3)
	p.G187S splice region variant LOF 65.6%	1 (3)
	p.P177S	1 (3)
	Loss unspecified	1 (3)
	Total	9 (26)
NRAS	Q61R	2 (6)
	p.Q61K missense (exon 3) GOF 21.9%	1 (3)
	p.Q61K missense (exon 3) GOF 16.6%	1 (3)
	Q61H	1 (3)
	p.Q61R missense (exon 3) GOF 51.9%	1 (3)
	p.G13D missense (exon 2) GOF 38.2%	1 (3)
	Q61K	1 (3)
	Total	8 (23)
PTEN	V166fs*14	1 (3)
	R130G-subclonal, H196fs*6, G251D	1 (3)
	Loss exons 4-9	1 (3)
	p.V166fs frameshift LOF 8.3%; p.D252G missense LOF 6.1%	1 (3)
	A137fs*42	1 (3)
	Total	5 (14)
SETD2	Q1638*	1 (3)
	Splice site 88-1G>A	1 (3)
	R620*	1 (3)
	R1492*	1 (3)
	Deletion exons 2-3	1 (3)
	Total	5 (14)

ARID2	p.R274*stop gain LOF 7.4% p.R542* stop gain LOF 32.9% p.G1658*stop gain LOF 16.3%; c.1581-1G>A splice region variant LOF 8.8% Total	1 (3) 1 (3) 1 (3) 3 (9)
CBL	Y371N R420Q P417S Total	1 (3) 1 (3) 1 (3) 3 (9)
IDH1	R132C p.R132G missense GOF 15.8% Total	2 (6) 1 (3) 3 (9)
MTAP	Loss unspecified Copy number loss Total	1 (3) 2 (6) 3 (9)
RAC1	P29S unspecified P29S subclonal p.P29S missense GOF 11.5% Total	1 (3) 1 (3) 1 (3) 3 (9)
APC	P1609L Loss exon 16 Total	1 (3) 1 (3) 2 (6)
ATM	P1382fs*6 K468fs*18 Total	1 (3) 1 (3) 2 (6)
CCND1	Amplification Amplification-equivocal Total	1 (3) 1 (3) 2 (6)
DNMT3A	Q696* p.Q656* stop gain LOF 35.8% Total	1 (3) 1 (3) 2 (6)
ERBB4	p.E452K missense GOF 37.7% E452K unspecified Total	1 (3) 1 (3) 2 (6)
FBXW7	L594F S426L, S582L Total	1 (3) 1 (3) 2 (6)
FGF12	E149K Total	1 (3) 1 (3)
FGFR2	R210Q N549K Total	1 (3) 1 (3) 2 (6)
FLT1	R281Q E72K Total	1 (3) 1 (3) 2 (6)
MEN1	R465* p.R98* stop gain LOF 12.8% Total	1 (3) 1 (3) 2 (6)
MSH6	p.F451fs frameshift LOF 49.9% F1104fs*1 Total	1 (3) 1 (3) 2 (6)
MUTYH	G382D p.Y179C missense LOF 48.7% Total	1 (3) 1 (3) 2 (6)
NOTCH1	p.FQ474 stop gain LOF 33.1% E455K Total	1 (3) 1 (3) 2 (6)
NPM1	583-2A>G splice site Loss unspecified Total	1 (3) 1 (3) 2 (6)
PIK3CA	R38H E542K Total	1 (3) 1 (3) 2 (6)

RAD21	Deletion exons 3-4 Amplification Total	1 (3) 1 (3) 2 (6)
RAF1	S257L Amplification Total	1 (3) 1 (3) 2 (6)
ROS1	P1440S E402K subclonal Total	1 (3) 1 (3) 2 (6)
SF3B1	G742D E902K Total	1 (3) 1 (3) 2 (6)
SPEN	S268fs*98 Q1757* Total	1 (3) 1 (3) 2 (6)
ABL1	ABL1-BCR non-canonical fusion	1 (3)
ARID1A	Q1519fs*13	1 (3)
ATRX	Deletion exons 9-10	1 (3)
BAP1	L633fs*4	1 (3)
BRCA2	S2670L	1 (3)
CARD11	D632N	1 (3)
CD70	R163*	1 (3)
CDK6	Amplification-equivocal	1 (3)
CDKN1B	p.Q141* stop gain LOF 11.0%	1 (3)
CHEK2	I157T	1 (3)
CIC	p.Q979 stop gain LOF 38.4%	1 (3)
CREBBP	Q1773*	1 (3)
CRKL	Amplification-equivocal	1 (3)
CTNNB1	S45F	1 (3)
DIS3	p.R780K missense GOF 35.8%	1 (3)
DDR1	R296C	1 (3)
EBF1	p.NQ195 stop gain LOF 17.5%	1 (3)
EGFR	S720F	1 (3)
ERCC3	p.K688K splice region variant LOF 31.5%	1 (3)
FAM46C	p.Q106 stop gain LOF 20.8%	1 (3)
FANCG	Rearrangement intron 13	1 (3)
FGF12	E149K	1 (3)
FGFR1	R445W	1 (3)
FLT3	M664I	1 (3)
GABRA6	W188*	1 (3)
GNA11	Q209L	1 (3)
GNAQ	Q209P	1 (3)
GRIN2A	p.W843* stop gain LOF 18.4%	1 (3)
HGF	E174K	1 (3)

IKZF1	p.Q149* stop gain LOF 29.5%	1 (3)
JAK2	V617F	1 (3)
KDM5C	Q706*	1 (3)
KDR	G494E	1 (3)
KMT2C (MLL3)	p.R2403 stop gain LOF 22.1%	1 (3)
KMT2D (MLL2)	R2734*	1 (3)
KRAS	V14I	1 (3)
LRP1B	c.8663-2A>C splice region LOF 45.9%	1 (3)
MAP2K1 (MEK1)	P124L	1 (3)
MITF	Amplification	1 (3)
MYC	Amplification	1 (3)
PARK2	G354R	1 (3)
PBRM1	p.E967 stop gain LOF 21.9%	1 (3)
PIK3C2G	E425K	1 (3)
PIK3R1	P194fs*12	1 (3)
PMS2	p.Q781 stop gain LOF 20.7%	1 (3)
PPP6C	p.P223S missense LOF 15.2%; p.R301C missense LOF 10.0%	1 (3)
PRKN	p.K427* stop gain LOF 25.2%	1 (3)
PTCH1	Splice site 3306_3306+1GG>AA	1 (3)
PTPRT	c.2370-1G>A splice region variant LOF 28.7%	1 (3)
RAD51D	W268*	1 (3)
RAD54L	E469*	1 (3)
RB1	Splice site 1128-2A>T, C553*	1 (3)
RICTOR	Amplification	1 (3)
RUNX1	c.97+1G>A splice region LOF 13.7%	1 (3)
SLIT2	p.C1385* stop gain LOF 26.4%	1 (3)
SNCAIP	W574*	1 (3)
STK11	L282fs*3	1 (3)
SUZ12	p.K341fs frameshift LOF 11.6%	1 (3)
TBX3	P646S	1 (3)
WT1	M1I	1 (3)

Abbreviations: del, deletion; GOF, gain of function; LOF, loss of function.