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Genomic and Molecular Analysis of Myelofibrosis Patients who Received Momelotinib and Pacritinib at Moffitt Cancer Center

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INTRODUCTION

- Pacritinib (PAC) and momelotinib (MMB) are less myelosuppressive JAK2 inhibitors that have been recently approved in myelofibrosis (MF) for thrombocytopenia and anemia, respectively
- Overlap in efficacy profiles show the ability to improve spleen volume and disease-related symptoms while favorably impacting anemia and thrombocytopenia

AIM

- To review patients seen at Moffitt Cancer Center who received either PAC and/or MMB to better understand the similarities and differences of patients receiving these agents after their respective approvals

METHOD

- 47 patients with MF who were treated at Moffitt Cancer Center with MMB or PAC were reviewed
- Demographic information, baseline blood counts, cytogenetics, genomic mutations, and prior therapy at initiation of MMB or PAC were collected
- T-tests and chi-square tests were conducted for statistical analysis

RESULTS

- MMB- and PAC-treated patients were moderately anemic at baseline (mean Hgb 8.8 g/dL and 9.1 g/dL, respectively)
- MMB-treated patients trended to have higher WBC counts (16.0 vs 8.9; p-value 0.13) and PLT counts (182 vs 115; p-value 0.097)
- PAC-treated patients harbored more mutations than MMB-treated patients (3.2 vs 2.3; p-value of 0.029)
- MMB-patients were less likely to have *JAK2* (50% vs 82%; p-value 0.037) mutations and more likely to have MPL mutations (23% vs 0%; p-value 0.035)
- Average of 2.7 vs 2.9 prior lines of therapy with MMB and PAC
- Among 8 patients who received both MMB and PAC, 7 received PAC first. The vast majority (95%) of patients were started at full dose (PAC: 200mg BID, MMB: 200mg daily)
- Reasons for starting less than full dose included drug-drug interactions (n = 2) and impaired kidney function (n = 1)

		MMB	PAC	ALL	
	N	30	25	47	P-Values
Demographics	Gender	M=50%, F= 50%	M=48%, F = 52%	M=49%, F = 51%	
	Age	74, (SD 7.9)	75, (SD 6.8)	75, (SD 7.7)	
PMF vs Post-ET/Post-PV MF		PMF = 60%	PMF = 60%	PMF = 64%	
Baseline Blood Counts	HGB	8.8, (SD 1.2)	9.1, (SD 1.6)	8.9, (SD 1.3)	0.325
	WBC	16.0, (SD 22.1)	8.9, (SD 7.3)	12.9, (SD 17.5)	0.133
	PLT	182, (SD 138)	115, (SD 154)	153, (SD 148)	0.097
	Peripheral blasts	0.4, (SD 0.9)	0.1, (SD 0.1)	0.3, (SD 0.8)	
Genomics	# of mutations	2.3, (SD 1.3)	3.2, (SD 1.7)	2.8, (SD 1.5)	0.029
	JAK2	50%	82%	68%	0.036
	CALR	27%	12%	19%	0.234
	MPL	23%	0%	10%	0.035
	ASXL1	37%	40%	40%	
	U2AF1	14%	29%	21%	0.226
	SRSF2	3%	4%	3%	
	TET2	0%	24%	15%	0.016
	SF3B1	10%	12%	11%	
	KRAS	3%	12%	6%	0.406
	High risk mutations	45%	53%	49%	0.642

		MMB	PAC	ALL	
Cytogenetics	Normal: 46, XX/XY	40%	40%	40%	P-value
	del20q	30%	28%	28%	
	del13q	7%	4%	6%	
	del Y	3%	8%	6%	
Prior Therapies	# of lines of therapy	2.7, (SD 1.9)	2.9, (SD 2.0)	2.6, (SD 1.7)	
	Jakafi	90%	92%	85%	
	Hydrea	43%	44%	38%	
	Danazol	20%	24%	23%	
	Thalidomide	17%	20%	23%	
	Peg-IFN	20%	24%	17%	
	Fedratinib	7%	16%	11%	
	Anagrelide	13%	4%	9%	
	Luspatercept	7%	8%	6%	
Transfusion Dependent Percentage		60%	72%	60%	0.351

CONCLUSIONS

- While there is considerable overlap in the patient populations receiving PAC and MMB since approval, there were subtle differences in terms of baseline laboratory and genomic characteristics
- Ongoing evaluation in a large, multi-center, real world database of PAC and MMB-treated patients may help optimize treatment selection in patients with cytopenic MF

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FUTURE CONSIDERATIONS

Further exploration of these cohorts may help to understand differential clinical activity when leveraged in the real-world setting

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