

# CALR mutation analysis is not indicated in patients with splanchnic vein thrombosis without evidence of a myeloproliferative neoplasm: a micro-review

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The recent discovery of exon 9 insertion and/or deletion mutations of the *CALR* gene in up to 80% of *JAK2*- and *MPL*-unmutated essential thrombocythemia and primary myelofibrosis patients compels the incorporation of *CALR* mutational analysis into the molecular diagnostic algorithm for these myeloproliferative neoplasms (MPN). MPN are a major cause of splanchnic vein thrombosis (SVT) which encompasses Budd-Chiari syndrome, portal and mesenteric vein thrombosis. Up to 40% of SVT patients are diagnosed with an overt or latent MPN [1]. While the MPN-associated *JAK2* V617F mutation is consistently reported in cohorts of SVT patients, several studies have investigated the role of *CALR* mutation analysis for MPN diagnosis in the presence of SVT with some debate existing [2-10]. Here, all reports published to date are summarized (Table 1). Briefly, of 944 patients studied only eight (0.8%) had evidence of a *CALR* mutation and of whom seven already had a previous diagnosis of an MPN.

MPN patients with *CALR* mutations have a significantly lower overall risk of thrombosis than their counterparts harboring the *JAK2* V617F and this is clearly the case with respect to SVT. While *CALR* mutated MPN patients may develop SVT, summarizing those published studies to date, routine investigation for these mutations appears not to be indicated in the diagnostic algorithm for SVT where no clinical or hematological features of an MPN are present.

## References

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Conflict of Interest: None

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Received 6 May 2016; accepted 12 May 2016; published online 10 June 2016

DOI: <http://dx.doi.org/10.20524/aog.2016.0057>

**Table 1** Summary of studies investigating *CALR* mutation status in splanchnic vein thrombosis

Reference	SVT patients	<i>JAK2</i> +	<i>CALR</i> +	<i>CALR</i> mutation	SVT site	MPN diagnosis
[2]	209	61/74 (82.4%) with MPN	4 (1.9%)	del 52 bp (n=3) / del 34 bp (n=1)	BCS (n=2) / PVT (n=2)	ET (n=3) / PMF (n=1)
[3]	144	27 (18.8%)	0 (0%)	-	-	-
[4]	29	27/29 (93.1%)	0 (0%)	-	-	-
[5]	66	12/66 (18.2%)	1 (1.5%)	del 5 bp	Not specified	Not specified
[6]	40	9/13 (69.2%) with MPN	0 (0%)	-	-	-
[7]	141	33/44 (75.0%) with MPN	1 (0.7%)	del 52 bp	PVT	PMF
[8]	132	39/45 (86.7%) with MPN	0 (0%)	-	-	-
[9]	83	24/83 (28.9%)	2 (2.4%)	del 52 bp (n=1) / Complex (n=1)	PVT (n=2)	ET (n=1) MPN-U (n=1)
[10]	100	2/100 (2.0%)	0 (0%)	-	-	-
Total	944		8 (0.8%)			

BCS, Budd-Chiari syndrome; ET, essential thrombocythemia; MPN, myeloproliferative neoplasms; MPN-U, myeloproliferative neoplasm-unclassified; PMF, primary myelofibrosis; PVT, portal vein thrombosis; SVT, splanchnic vein thrombosis