Neuberg DIAGNOSTICS

● India ● UAE ● South Africa ● USA

# Neu INSIGHTS

Neuberg DIAGNOSTICS CENTER FOR GENOMIC MEDICINE

# OncoCEPT HAEM

Serial number : 001 Edition : 1. 2022

# OncoCEPT - HAEM

- Sample Type:- Blood or Bone Marrow
- Next Generation Sequencing
- TAT:- 10 working days*

## GENES COVERED

- 40 key DNA target genes
- 29 driver genes
  (a broad fusion panel)

*for >90% samples

## List of Genes in Panel

### DNA

#### HOTSPOT GENES

| | | | |
|---|---|---|---|
| ABL1 | FLT3 | KIT | SETBP1 |
| BRAF | GATA2 | KRAS | SF3B1 |
| CBL | HRAS | MPL | SRSF2 |
| CEBPA | IDH1 | MYD88 | U2AF1 |
| CSF3R | IDH2 | NPM1 | WT1 |
| DNMT3A | JAK2 | PTPN11 | NRAS |

#### FULL GENES

| | | |
|---|---|---|
| ASXL1 | IKZF1 | SH2B3(LNK) |
| BCOR | NF1 | STAG2 |
| CALR | PHF6 | TET2 |
| ETV6 | PRPF8 | TP53 |
| EZH2 | RB1 | ZRSR2 |
| | RUNX1 | |

### RNA

#### FUSION DRIVER GENES

| | | | | |
|---|---|---|---|---|
| ABL1 | EGFR | JAK2 | MYBL1 | RARA |
| ALK | ETV6 (TEL) | KMT2A(MLL) | MYH11 | RBM15 |
| BCL2 | FGFR1 | MECOM | NTRK3 | RUNX1(AML1) |
| BRAF | FGFR2 | MET | NUP214 | TCF3(E2A) |
| CCND1 | FUS | MLLT10 | PDGFRA | TFE3 |
| CREBBP | HMGA2 | MLLT3 | PDGFRB | |

## CBC/BM findings under evaluation whenever a myeloid neoplasm is suspected (after ruling out other reactive/secondary causes):

1. Polycythemia
2. Cytopenia(Anaemia, leucopenia, thrombocytopenia)
3. Leukocytosis(Neutrophilia/eosinophilia/ monocytosis/basophilia)
4. Thrombocytosis
5. Acute leukaemia (blasts/atypical cells)
6. Dyspoiesis(Dyserythropoiesis/ dysgranulopoiesis/dysmegakaryopoiesis)
7. Ring sideroblasts
8. Myelofibrosis
9. Atypical lymphoid cells with hairy cytoplasmic projections
10. Rouleaux formation with lymphoplasmacytic cells

# Diseases Covered

## Disorder wise:

**1. Myeloproliferative Neoplasms**
- a. Polycythaemia Vera (PV)
- b. Primary Myelofibrosis (PMF)
- c. Essential thrombocythaemia (ET)
- d. Chronic myeloid leukemia, BCR-ABL1 positive
- e. Chronic neutrophilic leukaemia
- f. Chronic eosinophilic leukaemia, NOS
- g. Myeloproliferative Neoplasm, unclassifiable

**2. Mastocytosis**

**3. Myeloid/lymphoid neoplasms with eosinophilia & gene rearrangement**
- a. Myeloid/lymphoid neoplasms with PDGFRA rearrangement
- b. Myeloid/lymphoid neoplasms with PDGFRB rearrangement
- c. Myeloid/lymphoid neoplasms with FGFR1 rearrangement
- d. Myeloid/lymphoid neoplasms with PCM1-JAK2

**4.Myelodysplastic/myeloproliferative neoplasms**
- a. Chronic myelomonocytic leukaemia (CMML)
- b. Atypical chronic myeloid leukaemia, BCR-ABL1 negative (aCML)
- c. Juvenile myelomonocytic leukaemia (JMML)
- d. Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts & thrombocytosis
- e. Myelodysplastic/myeloproliferative neoplasm, unclassifiable (MDS/MPN-U)

**5. Myelodysplastic syndromes (MDS)**
- a. MDS with single lineage dysplasia
- b. MDS with ring sideroblasts
- c. MDS with multilineage dysplasia
- d. MDS with excess blasts
- e. MDS with isolated del(5q)
- f. MDS, unclassifiable
- g. Childhood myelodysplastic syndrome

**6. Myeloid neoplasms with germline predisposition** (CEBPA, RUNX1, ETV6, GATA2)

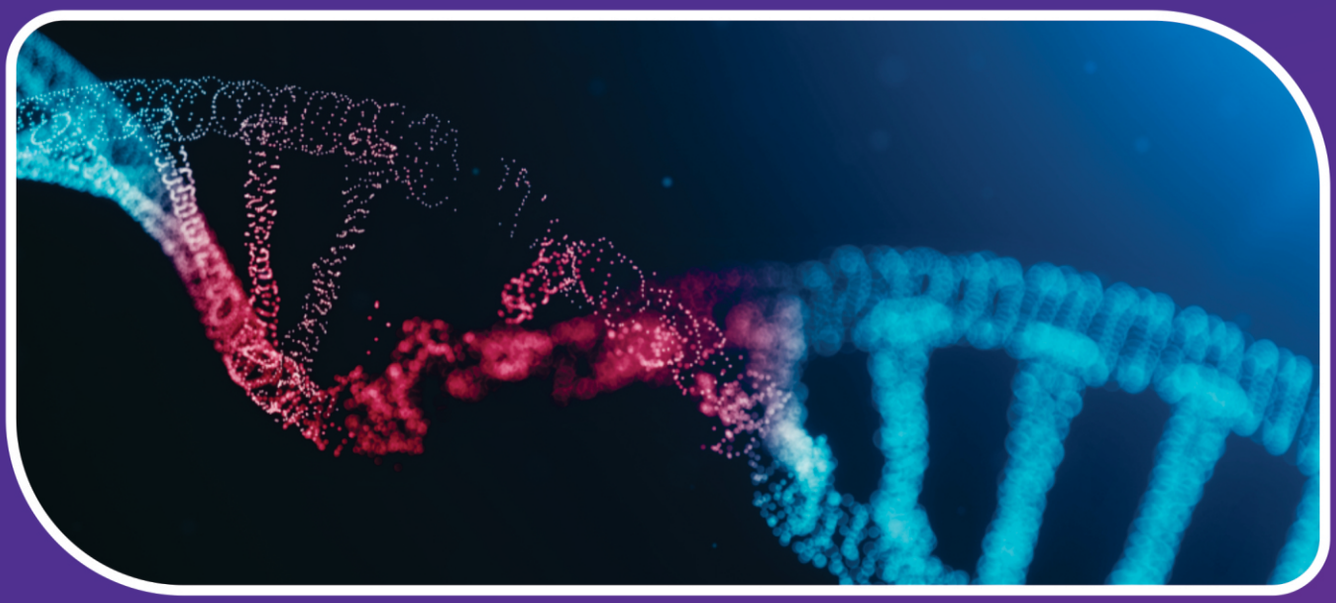
**7. Acute myeloid leukaemia(AML) & related precursor neoplasms**
- a. AML with t(8;21)/RUNX1-RUNX1T1
- b. AML with inv(16)/CBFB-MYH11
- c. AML with PMLRARA/variant RARA
- d. AML with t(9;11)/KMT2A-MLLT3 as well as other KMT2A rearrangements
- e. AML with t(6;9)/DEK-NUP214
- f. AML with t(1;22)/RBM15-MKL1
- g. AML with t(9;22)/BCR-ABL1
- h. AML with mutated NPM1
- I. AML with biallelic mutation of CEBPA
- j. AML with mutated RUNX1
- k. AML with myelodysplasia related changes
- l. Therapy related myeloid neoplasms
- m. AML, not otherwise specified
- n. Myeloid sarcoma

**8. Acute leukaemias of ambiguous lineage**
- a. Acute undifferentiated leukaemia
- b. Mixed phenotype acute leukaemia with t(9;22)/BCR-ABL1
- c. Mixed phenotype acute leukaemia with t(v;11q23.3)/KMT2A rearranged
- d. Mixed phenotype acute leukaemia, B/myeloid
- e. Mixed phenotype acute leukaemia, T/myeloid

**9. Precursor lymphoid neoplasms : B-lymphoblastic leukaemia/lymphoma (B-ALL/LBL)**
- a. B-ALL/LBL, not otherwise specified
- b. B-ALL/LBL with t(9;22)/BCR-ABL1
- c. B-2ALL/LBL with t(v;11q3.3)/KMT2A rearranged
- d. B-ALL/LBL with t (12;21) / ETV6-RUNX1
- e. B-ALL/LBL with t(1;19)/TCF3-PBX1
- f. B-ALL/LBL with ZNF384 related fusion

**10. Mature B-neoplasms**
- a. Chronic lymphocytic leukaemia (CLL)
- b. Hairy cell leukaemia (HCL) (BM sample preferred)
- c. Lymphoplasmacytic lymphoma/ Waldenstrom macroglobulinemia (LPL/WM) (BM sample preferred)

# Mutations (DNA)



## AML

| | | |
|---|---|---|
| NPM1 | FLT3-TKD | ASXL1 |
| CEBPA | TP53 | DNMT3A |
| RUNX1 | WT1 | IDH1 |
| KIT | TET2 | IDH2 |
| FLT3-ITD | Others | |

## MDS/MPN

| | | | |
|---|---|---|---|
| SF3B1 | SRSF2 | NRAS | ZRSR2 |
| JAK2 | DNMT3A | TP53 | STAG2 |
| MPL | U2AF1 | SETBP1 | IDH1 |
| CALR | TP53 | BCOR | IDH2 |
| TET2 | EZH2 | | Others |

## PMF

| | |
|---|---|
| JAK2 | IDH1 |
| MPL | IDH2 |
| CALR | SRSF2 |
| ASXL1 | SF3B1 |
| EZH2 | TET2 |

## CNL

| |
|---|
| CSF3R |
| SETBP1 |
| ASXL1 |
| JAK2 |

## CMML

| | |
|---|---|
| ASXL1 | NRAS |
| TET2 | CBL |
| SRSF2 | SETBP1 |
| RUNX1 | NPM1 |

## t-MNs

| | |
|---|---|
| TP53 | IDH2 |
| TET2 | NRAS |
| PTPN11 | FLT3 |
| IDH1 | |

## Mastocytosis

| | |
|---|---|
| KIT | CBL |
| TET2 | RUNX1 |
| SRSF2 | RAS family |
| ASXL1 | |

## JMML

| | |
|---|---|
| PTPN11 | CBL |
| KRAS | SETBP1 |
| NRAS | SH2B3 |
| NF1 | ASXL1 |

## MNGP

| | |
|---|---|
| CEBPA | GATA2 |
| RUNX1 | Same as JMML |
| ETV6 | CSF3R |

## CEL

| | |
|---|---|
| TET2 | EZH2 |
| ASXL1 | JAK2 |
| DNMT3A | KIT |

## TAM

| | |
|---|---|
| EZH2 | SH2B3 |
| JAK2 | RAS pathway genes |
| MPL | |

## PV

| |
|---|
| JAK2V617F |
| JAK2 exon 12 |
| SH2B3/LNK |

## ET

| |
|---|
| JAK2 |
| CALR |
| MPL |

## MDS

| | | |
|---|---|---|
| SF3B1 | RUNX1 | STAG2 |
| TET2 | U2AF1 | IDH1 |
| ASXL1 | TP53 | IDH2 |
| SRSF2 | EZH2 | CBL |
| DNMT3A | ZRSR2 | NRAS |
| | BCOR | Others |

## BPDCN

| | |
|---|---|
| TET2 | IDH2 |
| NPM1 | KIT |
| ASXL1 | RB1 |
| RAS family | BRAF |
| NRAS | TP53 |
| KRAS | |

## aCML

| |
|---|
| SETBP1 |
| CSF3R |

## APL

| |
|---|
| FLT3-ITD |
| FLT3-TKD |

- Acute myeloid leukaemia (AML)
- Primary Myelofibrosis (PMF)
- Therapy related myeloid neoplasms (t-MNs)
- Transient abnormal myelopoiesis(TAM)
- Chronic eosinophilic leukaemia (CEL)
- Acute promyelocytic leukaemia (APL)
- Chronic neutrophilic leukaemia (CNL)
- Mastocytosis
- Chronic myelomonocytic leukaemia (CMML)
- Juvenile myelomonocytic leukaemia (JMML)
- Myelodysplastic Syndrome / myeloproliferative neoplasms (MDS/MPN)
- Myelodysplastic Syndrome(MDS)
- Myeloid neoplasms with germline predisposition(MNGP)
- Atypical chronic myeloid leukaemia (aCML)
- Essential Thrombocythemia (ET)
- Polycythemia Vera (PV)
- Blastic plasmacytoid dendritic cell neoplasm(BPDCN)

# Fusions (RNA)

## Acute myeloid leukaemia(AML) and related precursor neoplasms

| | |
|---|---|
| RUNX1-RUNX1T1 t(8;21) | CBFB-MYH11 inv(16) |
| PML-RARA t(15;17) | DEK-NUP214 t(6;9) |
| RBM15-MKL1 t(1;22) | AML with BCR-ABL1 |

### KMT2A REARRANGEMENTS

| | | |
|---|---|---|
| MLLT3 t(9;11) | TET1 | CASP8AP2 |
| AFF1/AF4 | PICALM | CBL |
| MLLT1-ENL | ABI1 | CREBBP |
| MLLT10/AF10 | CASC5 | DCP1A |
| ELL | MYO1F | DCPS |
| PTD | SEPT5 | FNBP1 |
| MLLT4/AF6 | ACTN4 | GAS7 |
| EPS15 | FLNA | KIA1524 |
| MLLT11/AF1Q | FOXO3 | BTBD18 |
| SEPT9 | CEP170B | MYH11 |
| EPS15 | MAML2 | NEBL |
| SEPT6 | SEPT11 | NRIP3 |
| MLLT6/AF17 | ABI2 | PDS5A |
| AFF3/LAF4 | ACACA | SEPT2 |
| ARHGEF12 | AFF4/AF5 | SMAP1 |
| GMPS | ARHGEF17 | TOP3A |

## Acute promyelocytic leukaemia

### RARA REARRANGEMENTS: 3 types bcr1,bcr2,bcr3

- IRF2BP2-RARA
- NABP1-RARA t(2;17)
- TBL1XR1-RARA t(4;17)
- FIP1L1-RARA t(5;17)
- NPM1-RARA t(11;17)
- NUMA1-RARA
- ZBTB16-RARA t (11;17)
- ADAMTS17-RARA
- STAT5B-RARA
- PRKAR1A-RARA t(17;17)
- BCOR-RARA t(X;17)
- PML-RARA

## Chronic eosinophilic leukaemia

### ETV6 REARRANGEMENTS

- FLT3
- NTRK
- LYN
- SYK
- ABL1
- ETV6-JAK2
- BCR-JAK2

## Pediatric -AML

- RBM15-MKL1 t(1;22)
- KAT6A-CREBBP
- DEK-NUP214 t(6;9)
- KMT2A Rearrangements
- MLLT3
- MLLT10
- MLLT11

## B-lymphoblastic leukaemia/lymphoma

| | |
|---|---|
| t(9;22)/BCR-ABL1 | t(1;19)/TCF3-PBX1 |
| t(v;11q23.3)/KMT2A | ZNF384 related Fusions |
| t(12;21) /ETV6-RUNX1 | Others |

## Chronic myeloid leukaemia

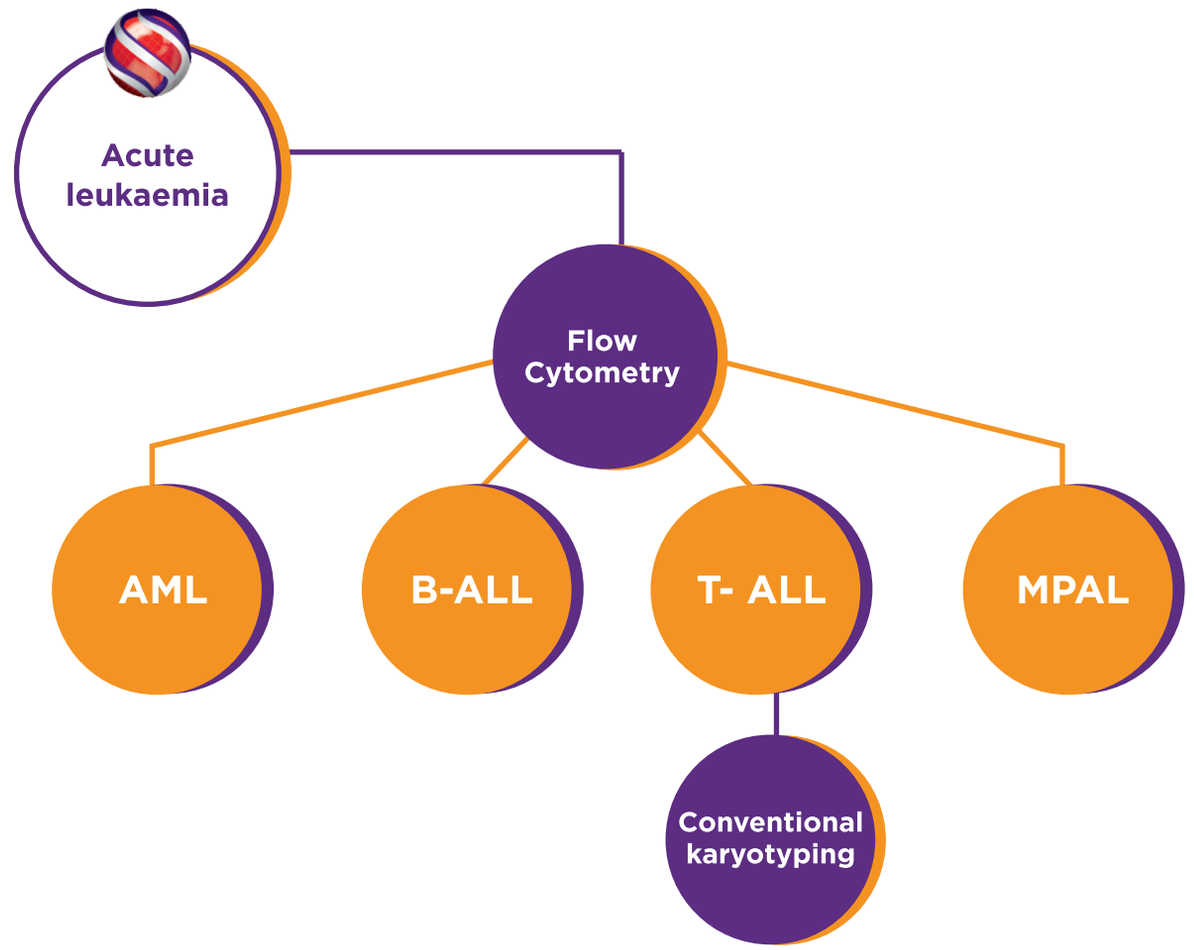
- BCR-ABL1

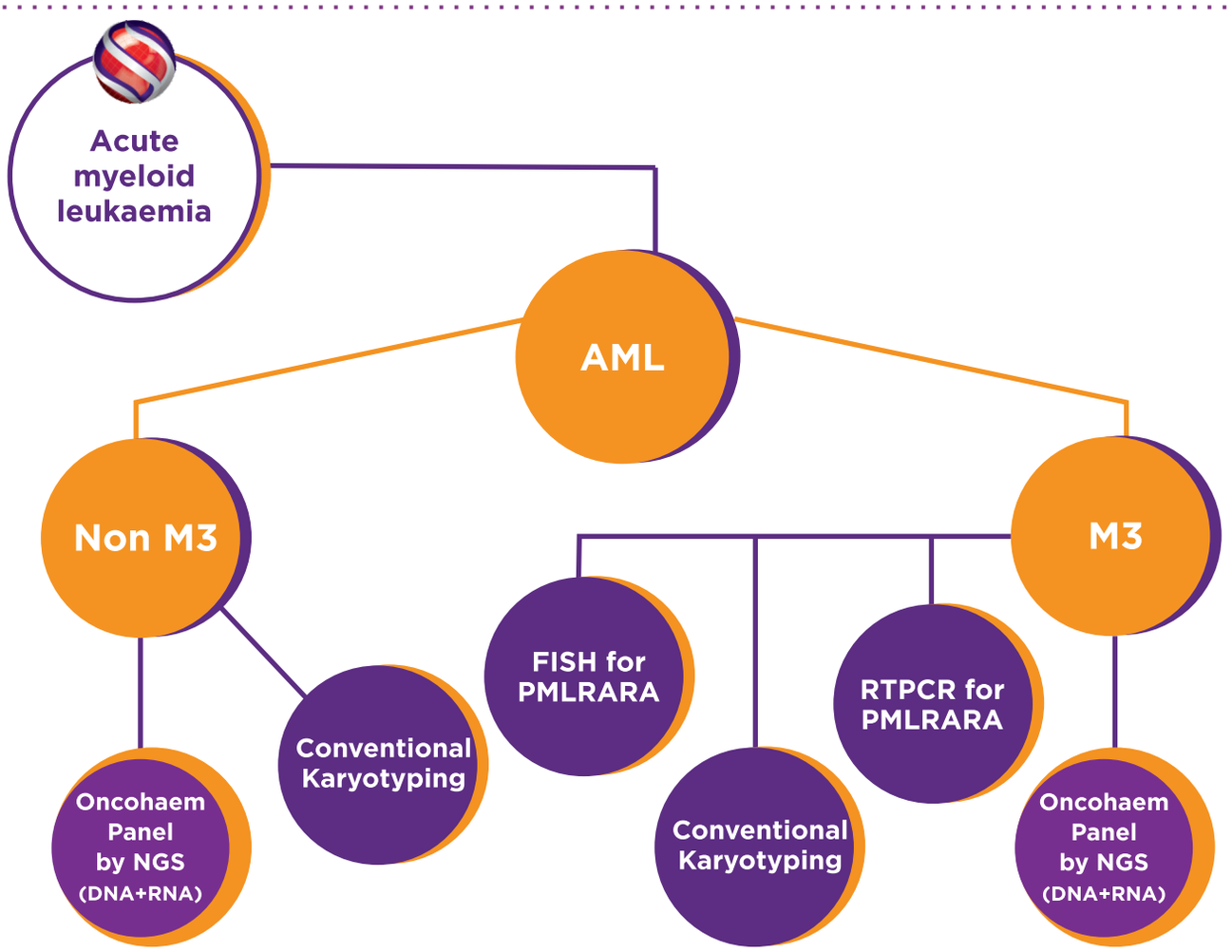
## Myeloid/lymphoid neoplasms with eosinophilia & gene arrangement

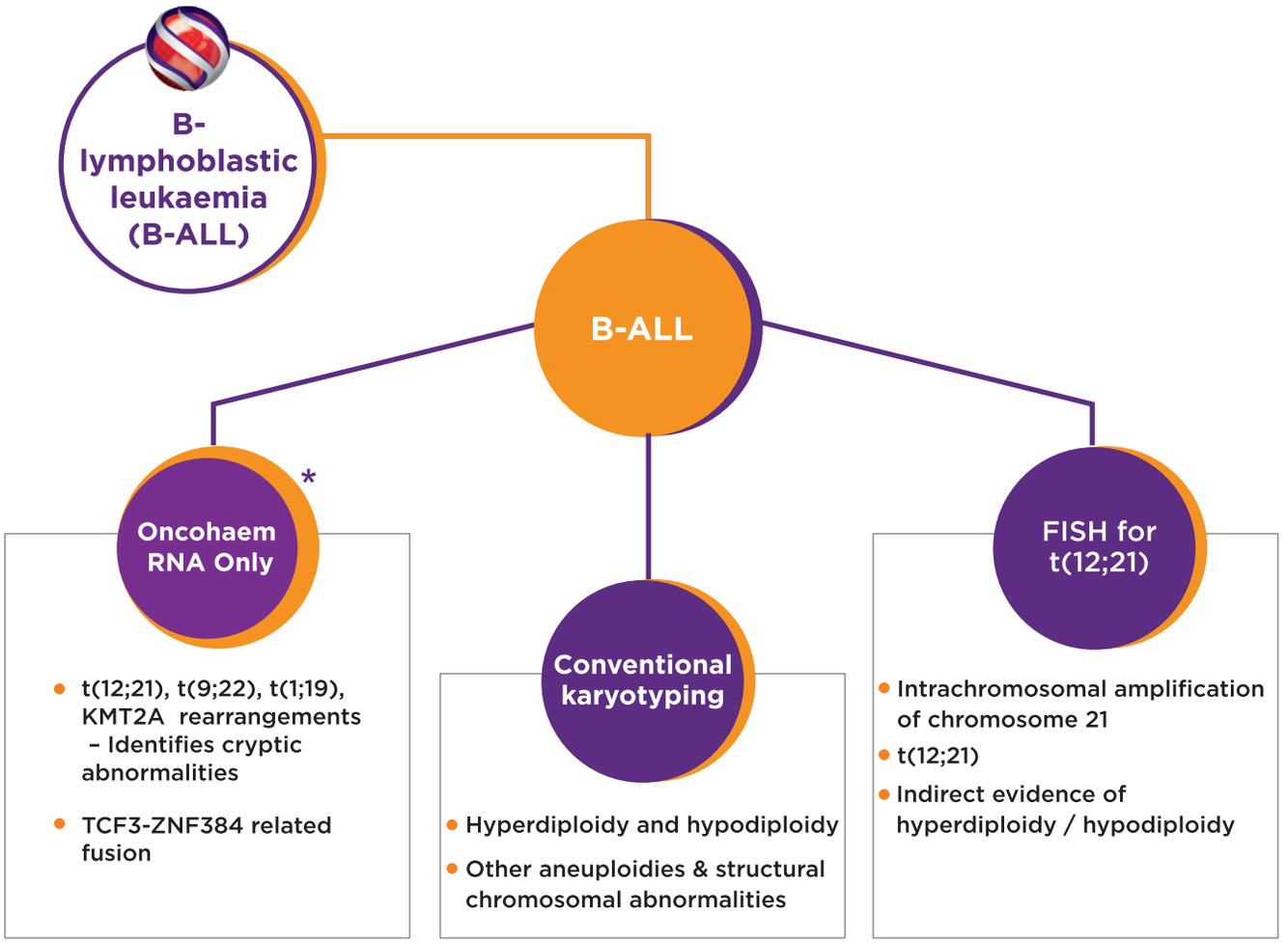
| PDGFRB REARRANGEMENTS | GOLGA4 | FGFR1 REARRANGEMENTS | JAK2 REARRANGEMENTS |
|---|---|---|---|
| CCDC6 | TNIP1 | ZMYM2 | PCM1 |
| SART3 | HIP1 | CNTRL | ETV6 |
| GIT2 | KANK1 | FGFR1OP | BCR |
| ERC1 | MYO18A | BCR | PAXC |
| BIN2 | COL1A1 | MYO18A | PDGFRA REARRANGEMENTS |
| NIN | DTD1 | TRIM24 | ETV6 |
| CCDC88C | GOLGB1 | FGFR1OP2 | FIP1L1 |
| TP53BP1 | CEP85L | TPR | KIF5B |
| NDE1 | TRIP11 | RANBP2 | CDK5RAP2 |
| RABEP1 | MPRIP | LRRFIP1 | STRN |
| SPECC1 | CPSF6 | CUX1 | FOXP1 |
| ETV6 | TPM3 | CPSF6 | TNKS2 |
| WDR48 | PDE4DIP | SQSTM1 | BCR |
| CAPRIN1 | PRKG2 | | |

# Bone Marrow Examination Is Must For All Suspected Myeloid Neoplasms

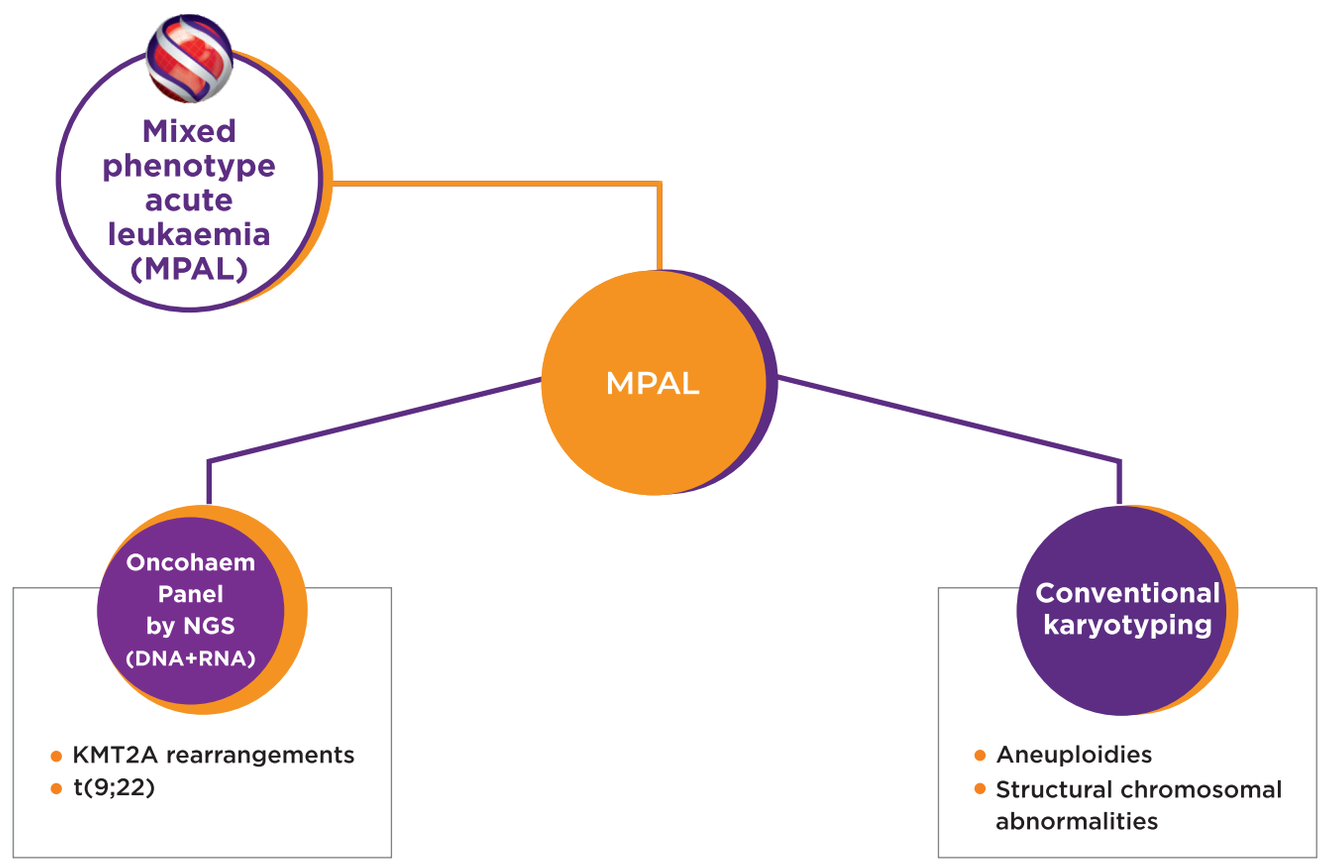
**(except under special circumstances)**



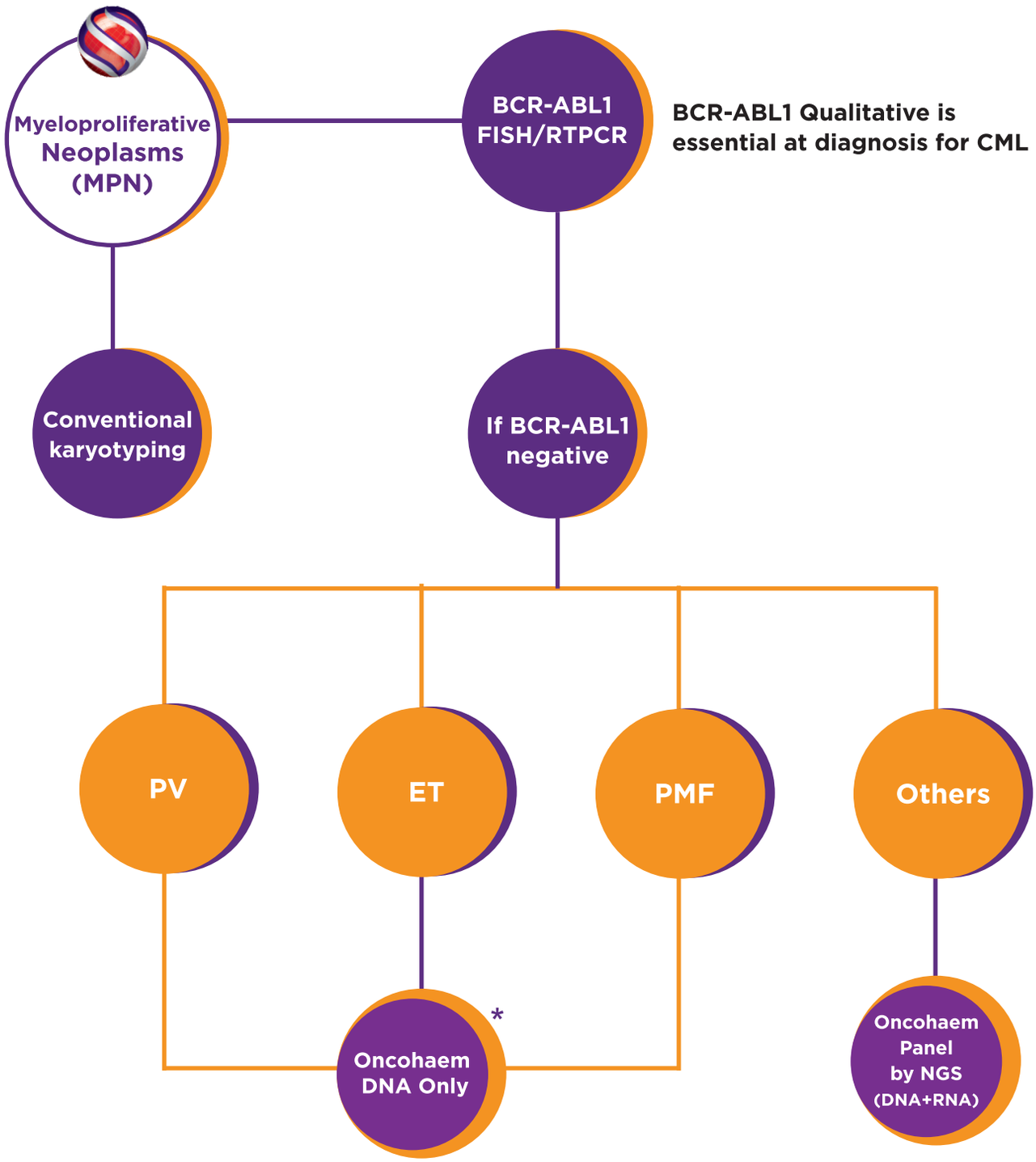






* Ideally Oncohaem panel by NGS (DNA + RNA)



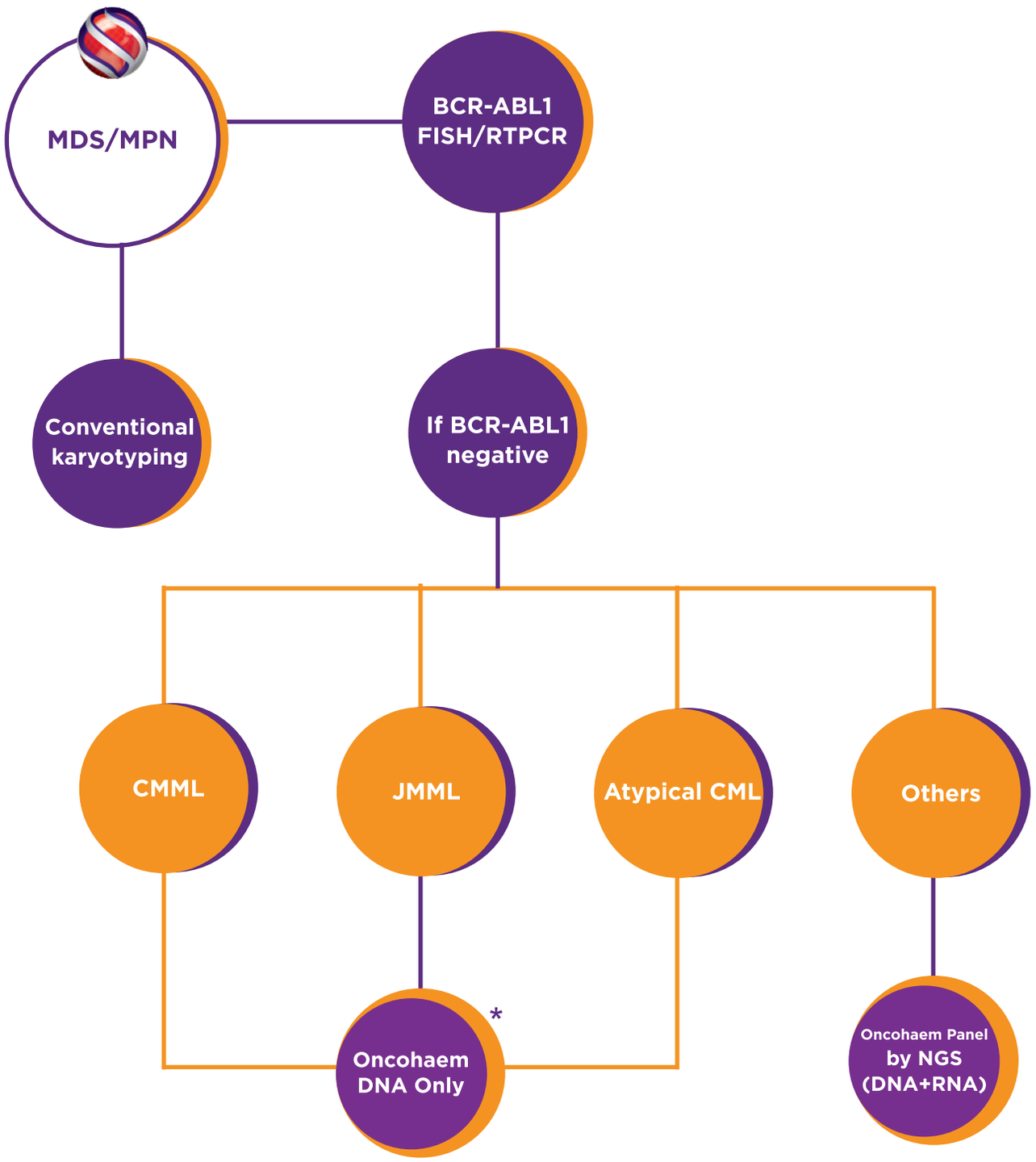
# Myeloproliferative Neoplasms (MPN)




*Ideally Oncohaem panel by NGS (DNA + RNA)

- Chronic myeloid leukaemia(CML)
- Polycythaemia Vera(PV)
- Primary Myelofibrosis(PMF)
- Essential Thrombocythaemia(ET)
- Chronic neutrophilic leukaemia(CNL)
- Chronic eosinophilic leukaemia(CEL)
- MPN-U

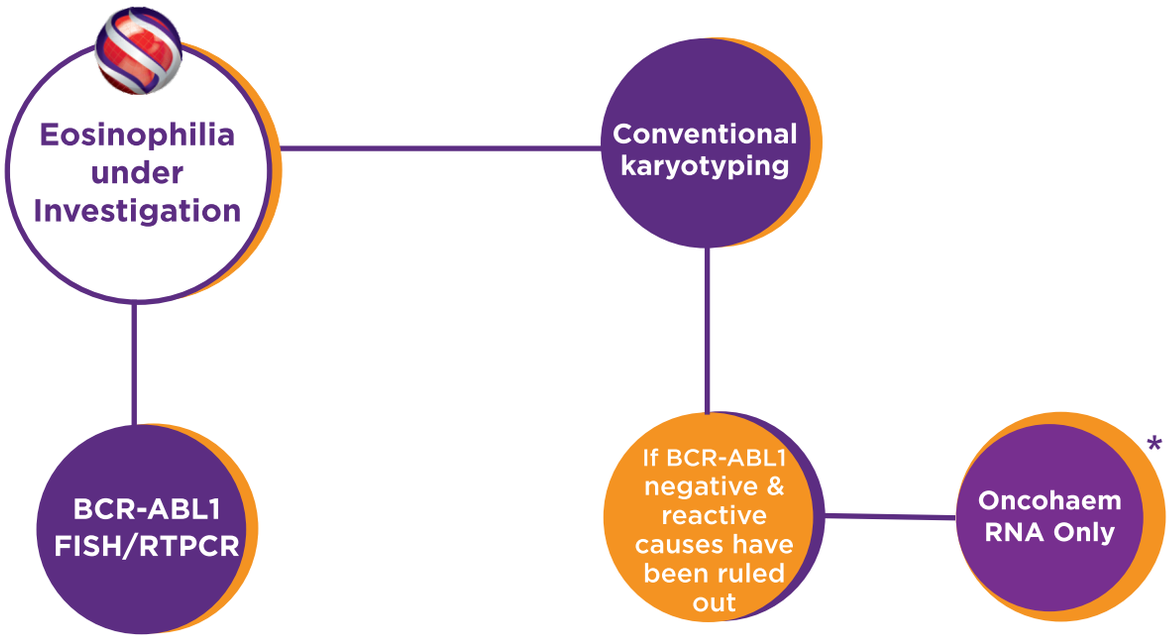
# Myelodysplastic syndrome/ Myeloproliferative neoplasm(MDS/MPN)




*Ideally Oncohaem panel by NGS (DNA + RNA)

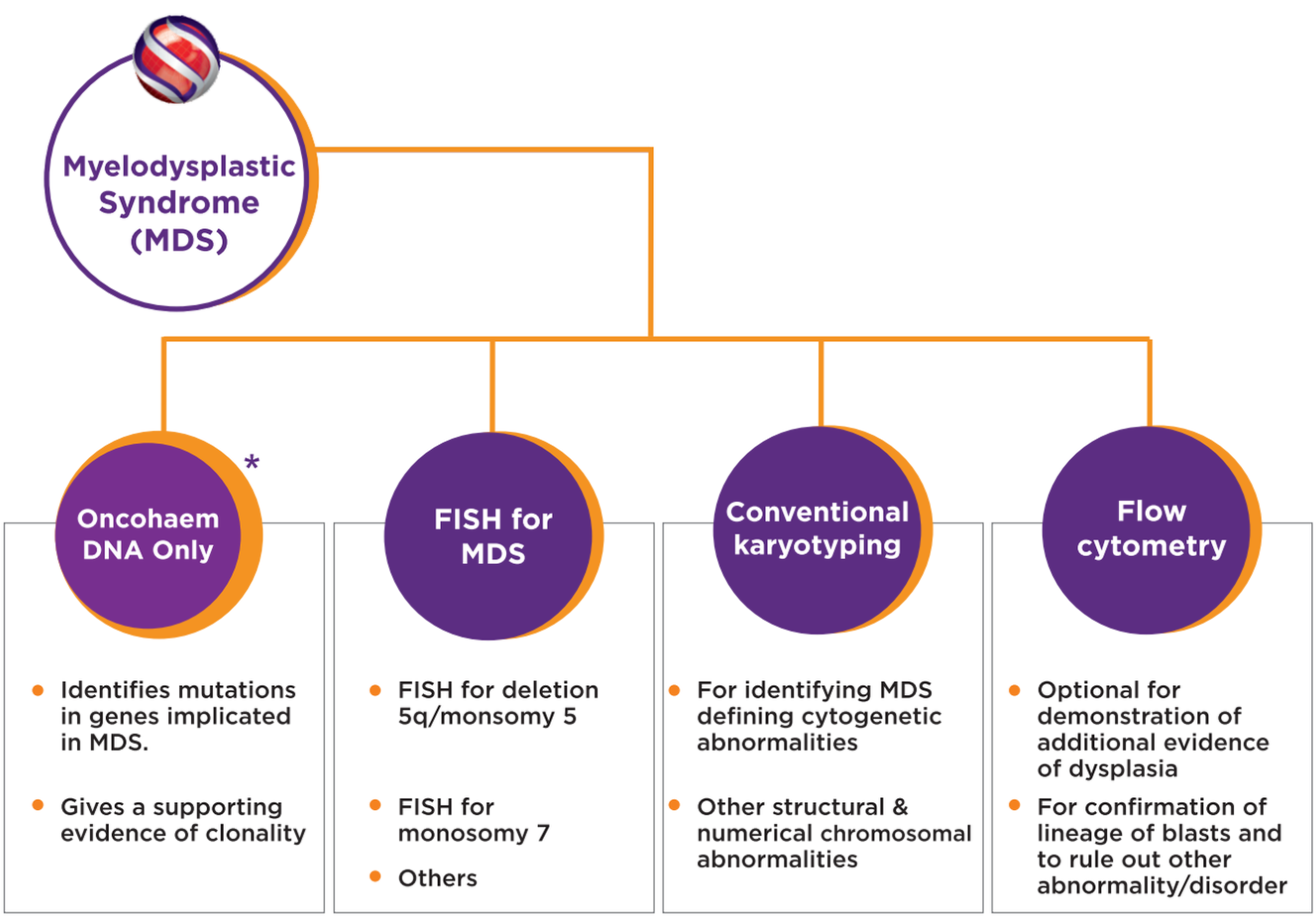
- Chronic myelomonocytic leukaemia(CMML)
- Atypical CML(aCML)
- Juvenile myelomonocytic leukaemia(JMML)
- MDS/MPN-RS-T
- MDS/MPN-U

# Eosinophilia under Investigation




*Ideally Oncohaem panel by NGS (DNA + RNA)

# Myelodysplastic Syndrome (MDS)




*Ideally Oncohaem panel by NGS (DNA + RNA)

# Chronic lymphocytic Leukaemia (CLL)


**Flow cytometry**

- For confirmation of Chronic lymphocytic leukaemia & exclusion of other Non Hodgkin lymphoma

**FISH for CLL**

- Especially for del(17P)(TP53)
- For knowing other abnormalities like del(13q), trisomy 12, del(11q), etc

**Oncohaem DNA Only** *

- For knowing TP53 mutation (for prognostication) as well as mutations in SF3B1 and MYD88 genes
- (TP53 mutation and FISH for Tp53 deletion are different)

**IGVH mutation analysiis**

- For prognostication

# Other Disorders


**Flow cytometry**

- Bone marrow sample is required

**Oncohaem DNA only for MYD88 mutation analysis**


**Flow cytometry**

- Bone marrow sample is required

**Oncohaem DNA only for BRAF V600E mutation analysis**

- **Hairy cell leukaemia(HCL)**
- **Waldenstrom Macroglobulinemia/Lymphoplasmacytic lymphoma(WM/LPL)**

Current analysis of hematological malignancies involves multiple sequential tests and laborious workflows. Adoption of next-generation sequencing (NGS) methods into clinical research laboratories has created an unprecedented opportunity to profile the multiple relevant driver genes in myeloid malignancies. Targeted NGS assay is designed to assist in the understanding of myeloid cancers. Specifically, it interrogates all relevant DNA mutations and fusion transcripts associated with myeloid disorders in a single NGS run.

## Why OncoCEPT - HAEM?

- Targetable fusions/rearrangements like PDGFRA, PDGFRB, etc. can be checked
- Rare transcripts, which are not regularly checked or are usually missed, can also be detected. e.g. ETV6-JAK2 and ETV6-FLT3 can be found in CEL which can be detected by this technique.
- Transcripts that are cryptic can also be detected, which karyotyping may fail to identify.
- Fusions resulting from translocations can be confirmed. e.g. not all translocations characterized as t(5;12)(q31-33;p12) lead to ETV6-PDGFRB fusion.
- Fusions suspected but not found by karyotyping can be detected.
- Multiple fusions of a particular gene can be seen, whereas, FISH can only detect a particular translocation depending upon the probe used.
- Testing individually for each fusion by FISH is expensive , however, here, whole panel can be covered in a very reasonable rate.
- Mutations other than FLT3, JAK2, NPM1 & CEBPA are also covered like – IDH2, DNMT3A, etc.
- A suspected case can be confirmed if mutation can be found. e.g. a suspected case of JMML having a mutation KRAS can confirm the diagnosis.
- Drugs are now available that can be used to target the mutations. e.g. IDH1 inhibitor.
- Mutations can help in knowing the prognosis of the disease. e.g. TP53 mutation in AML carries adverse prognosis.

# Our Services

Inherited Genetic Disorder

Reproductive Genetics

Cancer Genomics

Haemato Oncology

Transplant Immunology

Infectious Disorders

Pharmacogenomics

Research Services

# Notes :

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