

# Myeloproliferative neoplasms (MPN)

**Guide to the completion of the EBMT data collection form:  
MPN\_v2.0**

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**EBMT Registry**

EBMT Clinical Research & Registry Department



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## Introduction

Please make sure you have already checked the **Introduction to the EBMT Registry Completion Guidelines** document latest version available under *Manuals and Reference Documents* section on [EBMT website](#).

### Myeloproliferative neoplasms (MPN)

MPN include a group of haematological disorders originating from a pluripotent stem cell of haematopoiesis that typically present with a hypercellular bone marrow with fibrosis, hepatomegaly, splenomegaly, and increased blood cell counts (cytopenias are possible). With advanced disease the cellularity may decrease, fibrosis becomes predominant, blood counts may be low and the patient may be transfusion dependent. The transformation from one entity to another is not uncommon, as is the case with the transition from polycythaemia vera (PV) or essential or primary thrombocythaemia (ET) to myelofibrosis (MF). Moreover, all these conditions have an inherent tendency to progress to acute leukaemia.

In addition, myeloproliferative neoplasms have specific mutations: to distinguish these forms from CML, all forms should be BCR::ABL1 negative. More than 90% of PV patients and about 50% of primary MF and ET patients carry the JAK2 V617F mutation. FIP1L1-PDGFR $\alpha$  mutation can be found in hyper eosinophilic syndrome (HES), whereas c-kit mutation is found in systemic mastocytosis in around 85% of cases.

This form must be completed for all patients whose primary disease for which the HCT/CT/GT/IST treatment is being given is MPN.

No data items should be left blank unless specifically stated in the definition.

## Disease

### Date of diagnosis

Report the date of the first pathological diagnosis of the disease. This is the date when the sample was collected for examination or (in its absence) the date indicated by a physician within the patient's medical record.

### MPN Classification (WHO 2022)

Select the subclassification that is appropriate for the MPN.

Please see table 1 for definitions of the MPN subclassifications according to WHO 2022 (1).

Name	Diagnostic criteria
Primary myelofibrosis (overt PMF)	<p><i>Meeting all three major criteria and at least one minor criterion</i></p> <p>Major criteria:</p> <ol style="list-style-type: none"> <li>1. Megakaryocyte proliferation and atypia<sup>1</sup> and <math>\geq</math> grade 2 reticulin/collagen fibrosis</li> <li>2. Not meeting WHO criteria for other myeloid neoplasms</li> <li>3. Presence of JAK2, CALR, <u>or</u> MPL mutation <u>or</u> presence of another clonal marker or absence of evidence for reactive bone marrow fibrosis</li> </ol> <p>Minor criteria:</p> <ol style="list-style-type: none"> <li>1. Anaemia not otherwise attributed</li> <li>2. Leukocytosis <math>\geq 11 \times 10^9/L</math></li> <li>3. Palpable splenomegaly</li> <li>4. Increased lactate dehydrogenase (LDH), above upper limit</li> <li>5. Leukoerythroblastosis</li> </ol>
Primary myelofibrosis (prePMF)	<p><i>Meeting all 3 major criteria, and at least 1 minor criterion</i></p> <p>Major criteria:</p> <ol style="list-style-type: none"> <li>1. Megakaryocytic proliferation and atypia, without reticulin fibrosis <math>&gt;</math> grade 1 (MF-1), accompanied by increased age-adjusted BM cellularity, granulocytic proliferation, and often decreased erythropoiesis</li> <li>2. Not meeting the WHO criteria for BCR::ABL1<sup>+</sup> CML, PV, ET, myelodysplastic syndromes, or other myeloid neoplasms</li> <li>3. Presence of JAK2, CALR, or MPL mutation or in the absence of these mutations, presence of another clonal marker,<sup>2</sup> or absence of minor reactive BM reticulin fibrosis<sup>3</sup></li> </ol> <p>Minor criteria:</p> <p>Presence of at least 1 of the following, confirmed in 2 consecutive determinations:</p>

<sup>1</sup> Megakaryocytes with aberrant nuclear/cytoplasmic ratio and hyperchromatic and irregularly folded nuclei and dense clustering

<sup>2</sup> In the absence of any of the 3 major clonal mutations, the search for the most frequent accompanying mutations (eg, ASXL1, EZH2, TET2, IDH1/IDH2, SRSF2, SF3B1) are of help in determining the clonal nature of the disease.

<sup>3</sup> Minor (grade 1) reticulin fibrosis secondary to infection, autoimmune disorder or other chronic inflammatory conditions, hairy cell leukaemia or other lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathies.

	<ul style="list-style-type: none"> <li>a. Anaemia not attributed to a comorbid condition</li> <li>b. Leukocytosis <math>\geq 11 \times 10^9/L</math></li> <li>c. Palpable splenomegaly</li> <li>d. LDH increased to above the upper normal limit of institutional reference range</li> </ul>
Polycythaemia vera (PV)	<p><i>Meeting all three major criteria or the first two major criteria and one minor criterion</i></p> <p>Major criteria:</p> <ul style="list-style-type: none"> <li>1. Haemoglobin (Hb) &gt; 16.5 g/dL/16 g/dL (men/women) <u>and/or</u> Haematocrit (Hct) &gt; 49%/48% (men/women)</li> <li>2. Bone marrow (BM) tri-lineage hyperplasia (panmyelosis) with pleomorphic mature megakaryocytes<sup>4</sup></li> <li>3. Presence of JAK2 mutation (JAK2 p.V617F or JAK2 exon 12 mutations)</li> </ul> <p>Minor criterion:</p> <ul style="list-style-type: none"> <li>1. Subnormal serum erythropoietin level</li> </ul>
Essential or primary thrombocythaemia (ET)	<p><i>Meeting all four major criteria or first three major criteria and one minor criterion</i></p> <p>Major criteria:</p> <ul style="list-style-type: none"> <li>1. Platelet count <math>\geq 450 \times 10^9/L</math></li> <li>2. BM megakaryocyte proliferation with large and mature morphology and hyper-lobulated nuclei, Reticulin fibrosis grade should be <math>\leq 1</math></li> <li>3. Not meeting WHO criteria for other myeloid neoplasms</li> <li>4. Presence of JAK2, CALR or MPL mutation</li> </ul> <p>Minor criteria:</p> <ul style="list-style-type: none"> <li>1. Presence of a clonal marker or absence of evidence for reactive thrombocytosis</li> </ul>
Juvenile myelomonocytic leukaemia (JMML)	<p><b>I. Clinical and hematologic features (all 4 features mandatory)</b></p> <ul style="list-style-type: none"> <li>1. Peripheral blood monocyte count <math>\geq 1 \times 10^9/L</math></li> <li>2. Blast percentage in peripheral blood and bone marrow &lt;20%</li> </ul>

<sup>4</sup> BM biopsy may not be required if Hb > 18.5 g/dL in men or 16.5 in women (Hct > 55.5 in men and 49.5 in women).

	<ol style="list-style-type: none"> <li>3. Splenomegaly</li> <li>4. Absence of BCR::ABL1 rearrangement</li> </ol> <p><b>II. Genetic studies (1 finding sufficient)</b></p> <ul style="list-style-type: none"> <li>• Somatic mutation in PTPN11 or KRAS or NRAS</li> <li>• Clinical diagnosis of neurofibromatosis type 1 (NF1) or NF1 mutation</li> <li>• Germ line CBL mutation and loss of heterozygosity of CBL</li> </ul> <p><b>III. If none of the category II criteria are met, 2 of the following criteria must be fulfilled:</b></p> <ul style="list-style-type: none"> <li>• Any clonal cytogenetic abnormality</li> <li>• Fetal haemoglobin increased for age</li> <li>• Circulating myeloid precursors</li> <li>• GM-CSF hypersensitivity</li> <li>• White blood cell count <math>&gt;10 \times 10^9/L</math></li> </ul>
<p>Hyper eosinophilic syndrome (HES)</p>	<ol style="list-style-type: none"> <li>1. Peripheral blood hypereosinophilia – defined as <math>&gt; 1.5</math> eosinophils<math>\times 10^9/L</math> blood (<math>&gt;1500/mcl</math>) on two examinations at an interval of 1 month or greater– and/or – <ul style="list-style-type: none"> <li>• Tissue hypereosinophilia defined by the following:</li> <li>• Percentage of eosinophils in BM section exceeds 20% of all nucleated cells– and/or –</li> <li>• Pathologist is of the opinion that tissue infiltration by eosinophils is extensive– and/or –</li> <li>• Marked deposition of eosinophil granule proteins is found in the absence or presence of major tissue infiltration by eosinophils</li> </ul> </li> <li>2. Organ damage and/or dysfunction attributable to tissue hypereosinophilia</li> <li>3. Exclusion of other disorders or conditions as a major reason for organ damage</li> </ol>
<p>Chronic eosinophilic leukaemia (CEL)</p>	<ol style="list-style-type: none"> <li>1. Eosinophilia <math>\geq 1.5 \times 10^9/L</math></li> <li>2. Absence of the Ph chromosome, BCR::ABL1 fusion gene, and exclusion of other myeloproliferative (polycythaemia vera, essential thrombocytosis, primary myelofibrosis) or myelodysplastic-myeloproliferative (chronic myelomonocytic leukaemia, atypical chronic myelogenous leukaemia) neoplasms</li> <li>3. Absence of t(5;12)(q31-35;p13) or other PDGFRB gene rearrangements</li> <li>4. Absence of the FIP1L1-PDGFRB fusion gene or other PDGFRB gene rearrangements</li> <li>5. Absence of FGFR1 gene rearrangements.</li> </ol>

	<p>6. Less than 20% blasts in peripheral blood and BM, absence of <i>inv(16)(p13q22)</i>, <i>t(16;16)(p13;q22)</i>, or other features that warrant the diagnosis of AML</p> <p>7. Presence of a clonal or cytogenetic abnormality, &gt; 2% blasts in peripheral blood, or &gt; 5% blasts in BM</p>
<p>Chronic neutrophilic leukaemia (CNL)</p>	<p>1. PB WBC <math>\geq 25 \times 10^9/L</math>:        Segmented neutrophils plus band forms <math>\geq 80\%</math> of WBCs        Neutrophil precursors (promyelocytes, myelocytes, and metamyelocytes) &lt; 10% of WBC        Myeloblasts rarely observed        Monocyte count &lt; <math>1 \times 10^9/L</math>        No dysgranulopoiesis</p> <p>2. Hypercellular BM:        Neutrophil granulocytes increased in percentage and number        Neutrophil maturation appears normal        Myeloblasts &lt; 5% of nucleated cells</p> <p>3. Not meeting WHO criteria for <i>BCR::ABL1</i><sup>+</sup> CML, PV, ET, or PMF</p> <p>4. No rearrangement of <i>PDGFRA</i>, <i>PDGFRB</i>, or <i>FGFR1</i>, or <i>PCM1-JAK2</i></p> <p>5. Presence of <i>CSF3R</i> T618I or other activating <i>CSF3R</i> mutation <u>or</u>        In the absence of a <i>CSF3R</i> mutation, persistent neutrophilia (at least 3 months), splenomegaly, and no identifiable cause of reactive neutrophilia including the absence of a plasma cell neoplasm or, if present, demonstration of clonality of myeloid cells by cytogenetic or molecular studies</p>
<p>Aggressive systemic mastocytosis</p>	<p>Systemic mastocytosis (SM) diagnostic criteria plus "C" findings; no features of mast cell leukaemia</p> <p>Major criterion plus one minor criterion OR three minor criteria</p> <p>Major criterion:        Multifocal, dense infiltrates of mast cells (<math>\geq 15</math> mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organ(s)</p> <p>Minor criteria:</p> <ul style="list-style-type: none"> <li>● In biopsy sections of bone marrow or other extracutaneous organs, &gt;25% of the mast cells in the infiltrate are spindle-shaped or have atypical morphology, or of all mast cells in bone marrow aspirate smears, &gt;25% are immature or atypical</li> <li>● Detection of an activating point mutation at codon 816 of KIT in bone marrow, blood, or another extracutaneous organ</li> <li>● Mast cells in bone marrow, blood, or other extracutaneous organs express CD25, with or without CD2, in addition to normal</li> </ul>

	<p>mast cell markers</p> <ul style="list-style-type: none"> <li>• Serum total tryptase persistently exceeds 20 ng/mL (unless there is an associated clonal myeloid disorder, in which case this parameter is not valid)</li> </ul> <p>“C” findings:</p> <ul style="list-style-type: none"> <li>• Bone marrow dysfunction manifested by one or more cytopenia (ANC &lt;1 × 10<sup>9</sup>/L, Hb &lt;10 g/dL, or platelets &lt;100 × 10<sup>9</sup>/L) but no obvious nonmast cell hematopoietic malignancy</li> <li>• Palpable hepatomegaly with impairment of liver function, ascites, and/or portal hypertension</li> <li>• Skeletal involvement with large osteolytic lesions and/or pathologic fractures</li> <li>• Palpable splenomegaly with hypersplenism</li> <li>• Malabsorption with weight loss due to gastrointestinal mast cell infiltrates</li> </ul>
Systemic mastocytosis with an associated haematological neoplasm (SM-AHN)	<p>SM diagnostic criteria plus clonal haematologic disorder (eg, MDS, MPN, AML)</p> <p>Major criterion plus one minor criterion OR three minor criteria.</p> <p>Major criterion:</p> <p>Multifocal, dense infiltrates of mast cells (≥15 mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organ(s).</p> <p>Minor criteria:</p> <ul style="list-style-type: none"> <li>• In biopsy sections of bone marrow or other extracutaneous organs, &gt;25% of the mast cells in the infiltrate are spindle-shaped or have atypical morphology, or of all mast cells in bone marrow aspirate smears, &gt;25% are immature or atypical</li> <li>• Detection of an activating point mutation at codon 816 of KIT in bone marrow, blood, or another extracutaneous organ</li> <li>• Mast cells in bone marrow, blood, or other extracutaneous organs express CD25, with or without CD2, in addition to normal mast cell markers</li> <li>• Serum total tryptase persistently exceeds 20 ng/mL (unless there is an associated clonal myeloid disorder, in which case this parameter is not valid)</li> </ul>
Mast cell leukaemia	<p>Meets criteria for Systemic mastocytosis (SM). BM biopsy shows a diffuse infiltration, usually compact, by atypical, immature MCs. BM aspirate smears show 20% or more MCs.</p>
Mast cell sarcoma	<p>Local mast cell tumour with immature atypical mast cells and aggressive (invasive) growth pattern Cutaneous mastocytosis (CM) and SM criteria not fulfilled (CM and SM/Mast cell leukaemia excluded). High rate of recurrence/relapse. Resistance to therapy.</p>



MLN-TK with FGFR1 rearrangement	Evidence of myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK) defined by FGFR1 rearrangement
MLN-TK with PDGFRA rearrangement	Evidence of myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK) defined by PDGFRA rearrangement
MLN-TK with PDGFRB rearrangement	Evidence of myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK) defined by PDGFRB rearrangement
MLN-TK with JAK2 rearrangement	Evidence of myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK) defined by JAK2 rearrangement
MLN-TK with FLT3 rearrangement	Evidence of myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK) defined by FLT3 rearrangement
MLN-TK with ETV6::ABL1 fusion	Evidence of myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK) defined by ETV6::ABL1 fusion
MPN not otherwise specified (NOS)	Includes <b>MPN</b> -like neoplasms that cannot be clearly classified as one of the other subcategories of MPN

Table 1. WHO 2022 diagnostic criteria for MPN subclassification.

If the subclassification is not listed, check the box **Other** and specify the MPN classification (for example, MLN-TK with ETV6::FGFR2 fusion).

Note: If the disease has transformed to MF from ET or PV, then ET or PV should be registered as the diagnosis subclassification with the ET or PV date as the diagnosis date. The transformation to MF can be registered on the Disease status at main treatment form by using the subclassification Secondary myelofibrosis.

### Therapy-related MPN

Indicate if MPN developed due to medical treatment (therapeutic agents or radiation). Mark **Unknown** if this information is unavailable.

## MPN Assessments

### (Palpable) Spleen size

Indicate the size of the spleen in centimetres, measured below the costal margin as assessed by physical examination. Select **Not evaluated** if the spleen size was not assessed. If the value is unavailable, check **Unknown**.

If the patient underwent a splenectomy, report this via the 'Treatment non-HCT/CT/GT/IST' form.

### Spleen span on ultrasound or CT scan

Indicate the maximum diameter of the spleen in centimetres, as assessed by ultrasound or CT scan. Select **Not evaluated** if the spleen span was not assessed. If the value is unavailable, check **Unknown**.

If the patient underwent a splenectomy, report this via the 'Treatment non-HCT/CT/GT/IST' form.

### Transfusion dependency

Transfusion dependence is defined as the transfusion of at least 6 units of RBC in a 12-week period for a Hb level of <8.5 g/dL, in the absence of bleeding or treatment-induced anaemia (according to the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report).

Select **Yes** if the patient was transfusion dependent at time of the MPN diagnosis. Otherwise, check **No**. If the transfusion dependency status is unavailable, check **Unknown**.

### Bone marrow fibrosis

Bone marrow fibrosis represents the continuous replacement of blood-forming cells with excessive scar tissue diagnosed in a bone marrow trephine examination.

Indicate the degree of bone marrow fibrosis according to the European Consensus.

Grading	Description
Grade 0 (MF-0)	Scattered linear reticulin with no intersections corresponding to normal bone marrow
Grade 1 (MF-1)	Loose network of reticulin with many intersections, especially in perivascular areas
Grade 2 (MF-2)	Diffuse and dense increase in reticulin with extensive intersections, occasionally with only focal bundles of collagen and/or focal osteosclerosis

Grade 3 (MF-3)	Diffuse and dense increase in reticulin with extensive intersections with coarse bundles of collagen, often associated with significant osteosclerosis
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Table 2. Bone marrow fibrosis grading.

If the grade of bone marrow fibrosis was not assessed during the pathology examination, select **Not evaluated**. If the bone marrow fibrosis grading is unavailable, check **Unknown**.

### Blast count (peripheral blood)

Indicate the blast count in the peripheral blood in percentage (%). Select **Not evaluated** if the blast count was not assessed. If the value is unavailable, check **Unknown**.

### IPSS (myelofibrosis only)

International Prognostic Scoring System (IPSS) (2) estimates prognosis based on the following risk factors present at diagnosis:

- Age > 65 years
- Haemoglobin (Hb) < 10 g/dL
- WBC > 25×10<sup>9</sup>/L
- Peripheral blood blasts ≥ 1%
- Constitutional symptoms

IPSS is defined based on the total number of points of the patient (1 risk factor present = 1 point) as follows:

IPSS risk category	Total number of points	Proportion of patients, %	Median OS (years)
Low risk	0	22	11.25
Intermediate-1	1	29	7.9
Intermediate-2	2	28	4.0
High risk	≥ 3	21	2.25

Table 3. IPSS for MF.

If the IPSS was not assessed, select **Not evaluated**. If the IPSS is unavailable, check **Unknown**.

## DIPSS (myelofibrosis only)

The Dynamic International Prognostic Scoring System (DIPSS) (3) places a time-dependent risk evaluation over the original IPSS evaluation, generating a new prognostic score.

Prognostic factors	Points		
	0	1	2
Age (years)	≤ 65	> 65	
WBC (x 10 <sup>9</sup> /L)	≤ 25	> 25	
Haemoglobin (g/dL)	≥ 10		< 10
% Peripheral blood blasts	< 1	≥ 1	
Constitutional symptoms	No	Yes	

Table 4. DIPSS Prognostic Factors in MF.

IPSS risk category	Total number of points	Median OS (years)
Low risk	0	Not reached
Intermediate-1	1-2	14.2
Intermediate-2	3-4	4
High risk	5-6	1.5

Table 5. DIPSS risk assessment in MF.

If the DIPSS was not assessed, select **Not evaluated**. If the DIPSS is unavailable, check **Unknown**.

## MIPSS70 (myelofibrosis only)

The Mutation-Enhanced International Prognostic Scoring System (MIPSS70) is based on three genetic variables and six clinical risk factors present at diagnosis:

- Haemoglobin (Hb) < 10 g/dL
- WBC > 25×10<sup>9</sup>/L
- Platelets < 100×10<sup>9</sup>/L
- Peripheral blood blasts ≥ 2%
- Bone marrow fibrosis grade ≥ 2

- Constitutional symptoms
- Absence of CALR type 1/like mutation
- Presence of any high molecular risk (HMR) mutation, specifically ASXL1, SRSF2, EZH2, IDH1, or IDH2
- Presence of  $\geq 2$  HMR mutations

MIPSS70 risk category	Total number of points	Median OS (years)
Low risk	0-1	27.7
Intermediate	2-4	7.1
High risk	$\geq 5$	2.3

Table 6. MIPSS70 risk assessment inMF.

You can visit <http://www.mipss70score.it/> for the MIPSS70 calculation.

If the MIPSS70 was not assessed, select **Not evaluated**. If the MIPSS70 is unavailable, check **Unknown**.

## Chromosome analysis

### Chromosome analysis done before HCT/CT/IST treatment

In this section, describe the results of all chromosome analyses (all methods including FISH) performed at/after diagnosis but before the HCT/CT/IST treatment. If there were multiple chromosome analysis tests done on different dates, the results can be registered separately along with the test date.

Indicate if chromosome analysis was done or not before the HCT/CT/IST treatment. Check **Unknown** if it is not known whether it was performed.

### Output of analysis

Indicate if the output of the chromosome analysis will be reported as **separate abnormalities** or as a **full karyotype**.

### What were the results

**Normal** - the chromosome analysis has been performed and the results have been found normal

**Abnormal** - the chromosome analysis has been performed and abnormalities have been found. In addition, indicate the total number of different abnormalities present (**number of abnormalities present**).

**Failed** - the chromosome analysis was done but failed

### Date of chromosome analysis

Indicate the date of the chromosome analysis.

### Chromosome analysis details

Indicate for each abnormality in the table whether it was **Absent**, **Present**, or **Not evaluated**.

If a chromosome abnormality was checked, but not listed as an option in the table, select **Other** and specify the abnormality, marking whether it was **Absent** or **Present**.

### Transcribe the complete karyotype

If it is not possible to report the chromosome analysis results as per the abnormalities table please enter the complete karyotype. Describe all abnormalities according to the ISCN karyotype nomenclature. This notation includes the total number of chromosomes, the sex chromosomes, and any extra, missing or mutated autosomal chromosomes. For example, **47, XY, +18** indicates that the patient has 47 chromosomes, is a male, and has an extra autosomal chromosome 18.

## Molecular marker analysis

### Molecular marker analysis done before HCT/CT/IST treatment

In this section, describe the results of all molecular marker analyses (performed at/after diagnosis but before the HCT/CT/IST treatment). If there were multiple molecular marker analyses tests done on different dates, the results can be registered separately along with the test date.

Indicate if molecular marker analysis was done or not before the HCT/CT/IST treatment. Check **Unknown** if it is not known whether it was performed.

### Date of molecular marker analysis

Indicate the date of the molecular analysis. If there were multiple molecular tests done on different dates, the results can be registered separately along with the test date. For example, if the test date of the MPN driver mutations (JAK2, CALR, MPL) and the test date of additional somatic mutations (ASXL1, SRSF2 etc.) do not coincide.

## Molecular marker analysis details

If molecular marker analysis was performed, indicate for each marker in the table whether it was **Absent**, **Present** or **Not evaluated**.

If a molecular marker is detected, but not listed as an option in the table, select **Other** and specify the marker, indicating whether it was **Absent** or **Present**.

### CALR mutation

If **CALR** mutation is present, indicate the mutation type if known. CALR type 1 mutation is a 52-bp deletion (L367fs\*46) and CALR type 2 mutation is a 5-bp insertion (K385fs\*47). All other mutations can be categorised as type 1 like or type 2 like, depending on the extent of amino acid deletion. If the lab report does not specify the type, select **Present but type unknown**.

### TP53 mutation

If **TP53** mutation is present, indicate the mutation type if known. A TP53 mutation is considered a multi hit if it fulfils one of the following criteria

- 2 or more distinct mutations of TP53 with a VAF of  $\geq 10\%$
- 1 mutation and 1 deletion involving the TP53 locus
- 1 mutation with VAF  $\geq 50\%$
- 1 mutation with complex karyotype

A TP53 mutation is considered single hit if either one of the following criteria is fulfilled:

- a single TP53 mutation with VAF  $< 50\%$
- loss of 17p13 involving TP53 locus without TP53 mutations

If the lab report does not specify the type, select **Unknown**.

## Bibliography

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