

## Deep Insight Section

# Guidance for reporting the interpretation of cytogenomic test results in haematological neoplasms

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## Abstract

Deep insight on Guidance for reporting the interpretation of cytogenomic test results in haematological neoplasms

### **Relationship of any abnormalities found to the referral reason**

The report should include a description of the abnormality identified and the results should be interpreted with respect to the referral reason, or any subsequent information received regarding the patient (e.g. information subsequently communicated by referring clinician). For haematological samples the final diagnosis may or may not be known at time of sample collection and consequently the referral reason can be a confirmed

diagnosis, a presumptive diagnosis, a differential diagnosis or a description of clinical symptoms or findings.

- Where a diagnosis is confirmed, the report should state whether the result is consistent with this diagnosis. It is unhelpful to discuss the association of the abnormality with other disease entities as it may bring the diagnosis into question.

- Where the diagnosis is unconfirmed the report should state whether the result supports the proposed/presumptive diagnosis. When there is a differential diagnosis the report should discuss the result in relation to the different neoplasms considered.

- Where no specific diagnosis has been stated on the referral card, and only clinical information has been provided, it is advised to contact the clinician or the

pathology/haematology laboratory for more information before reporting. However, when this is not possible, the report should provide information on its association with specific disease entities.

- In some cases an abnormality may be identified that is inconsistent with the referral reason. It is known that some patients with a haematological malignancy have a second haematological neoplasm and it is not unusual in these cases to identify an abnormal clone containing recurrent abnormalities associated with one or both neoplasms. For example, in a patient referred for CLL, a clone with a deletion 20q may be detected. In such cases it is advised to contact the clinician for further information before reporting. However, when this is not possible, the report should state that the abnormality detected neither supports nor excludes the diagnosis indicated on the referral form and should provide information of any association with other specific disease entities. As a further example, in a patient referred for CLL, two independent clones may be detected, one with a trisomy 12 and one with a monosomy 7. Information pertaining to both abnormalities should be provided on the report.

- In some cases the abnormality detected may be suspected to have a constitutional rather than acquired origin and this should be discussed in the report. Depending on the nature of the abnormality, and considering any reproductive implications for the patient's extended family, confirmation of the patient's constitutional cytogenomic testing can be suggested.

- The most recent WHO (currently 2017) nomenclature should be used in relation to the disease category, where appropriate.

### **Reporting normal results**

The probability of detecting an abnormality depends on the pathology and methodology used. Laboratories should ensure that the most appropriate testing strategy is undertaken. Interpretation of normal test results needs careful consideration.

- Where an abnormal clone cannot be excluded, for example where insufficient metaphases have been obtained or cell enrichment is not optimal (such as low purity of CD138+), the report should include a statement to this effect. In addition, appropriate additional testing should be recommended in the report if not already undertaken.

Where a prognostic test is performed the report should clearly state that no high risk/ adverse prognostic factors were detected.

### **Reporting complex results**

Reporting complex test results can be challenging and it is important that the information provided is succinct and clear to the reader of the report.

The report should summarise the main diagnostic or prognostic abnormalities in a clear statement or in

tabular form, if possible near the beginning of the report.

- It should be clear which pertinent prognostic factors have been tested and the report should state whether high risk or established abnormalities have been detected or not detected (for example TP53 deletion or mutation not detected).

- The complex nature of the test result should be highlighted although a full description of all the abnormalities is not required. If included these should be listed elsewhere in the report so as not to detract from the major findings.

- Some pathologies, such as multiple myeloma, demonstrate high intraclonal variability and the FISH signal patterns observed can be very heterogeneous. It is recognised that such cases can be difficult to report and therefore complex signal patterns do not need to be described in detail. However, the report should state an atypical heterogeneous signal pattern was detected showing gene rearrangement, gain, loss or amplification.

### **Prognostic and predictive information**

It is good practice to include prognostic and predictive information in the report. However, it is recognised that local policy and national recommendations need to be taken into account when deciding whether to include this information in the report. For example, inclusion of this information may not be required when it will be summarised in an integrated multidisciplinary report or inclusion may be unhelpful in cases where the report is given directly to the patient. In the latter case, information regarding prognosis should be reported with caution as there are always exceptions on a patient level: e.g. cases with CLL and TP53 aberrations that do perform well, etc. Similarly, inclusion of predictive response to therapy in the report can be unhelpful as choice of adequate therapeutic option by the clinician needs to take into account the patients comorbidities and other clinical issues. Where laboratory policy is not to include this information in the report the laboratory may choose to make this information, and any new predictive data, available to the clinician outside the report (telephone, extra fact sheet, link to laboratory website, separate appendix).

Where prognostic information is included or has been specifically requested a prognostic statement must be provided.

- When no informative prognostic genetic biomarkers have been identified this should be stated.

- Where the prognostic information is currently contentious this should be highlighted and referenced in the report.

- Where the abnormality is a predictive marker for response to therapy it is recommended to mention it in the report.
- Prognostic information provided should relate to robust data from multiple publications/international trials/trial protocols or widely accepted prognostic systems exists (e.g. IPSS-R in MDS, ELN recommendations and MRC prognostic system in AML), or evidence from large randomised control trials of patients undergoing similar relevant treatment or meta-analysis/systematic review of multiple studies.
- Multiple concordant studies can be used and should be referenced.
- Small and isolated studies should not be used to derive prognosis although this information can be given in the report if put in context and referenced.
- It should be noted that the prognostic impact of a distinct marker relates to the specific treatment regimen used in the respective study, e.g. prognosis of APL with t(15;17)(q24;q21) is only favourable if treatment protocols including ATRA and/or arsenic trioxide are used.
- Cytogenomic results are just one component of establishing the patients overall prognosis. For some diseases a combined scoring system is used to establish risk that incorporates risk scores from multiple different tests. For these neoplasms it is recommended to state the cytogenetic risk score in the report to avoid any confusion with the overall risk score which may be different.

### **Recommendations**

Where additional testing, not already undertaken, is required to clarify the significance of the results this should be stated on the report.

### **Follow up testing**

The interpretation of follow up testing must relate the current results to the previous test results and the previous test reference number and sample date should be provided in the report.

### **Technical reports and provisional reports for discussion at multi discipline meetings**

In some circumstances a provisional or abbreviated report is issued prior to discussion at a multi-disciplinary team meeting (MDT) or before the results of other ongoing testing are available. If a purely technical report is issued it should be made clear that the interpretation of the results will be incorporated into a final integrated report.

## **References**

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*This article should be referenced as such:*

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