NICE advice

MMprofiler for prognostic risk classification in multiple myeloma

Medtech innovation briefing
Published: 10 August 2021

www.nice.org.uk/guidance/mib270

Summary

- The **technology** described in this briefing is MMprofiler. It is used for assessing the risk of disease progression in multiple myeloma.
- The **innovative aspects** are the unique SKY92 gene expression signature. This has been developed into a validated clinical test which the company claims could improve risk classification and result in more tailored drug treatment regimens.
- The intended **place in therapy** would be alongside standard care markers for newly diagnosed, relapsed or refractory multiple myeloma.
- The **main points from the evidence** summarised in this briefing are from 6 studies (3 secondary analyses with 2 based on randomised controlled trials, 1 analytical validation, 1 prospective case series, and 1 prospective single-arm trial) including 5,532 people. They show that MMprofiler (SKY92) can be effective as a prognostic marker for multiple myeloma.

- **Key uncertainties** around the evidence or technology are that several studies were secondary analyses validating MMprofiler as a prognostic marker for multiple myeloma. Further evidence is needed evaluating the use of MMprofiler in treatment decisions and its effect on clinical outcomes compared with standard care markers. Further prospective comparative research is also needed on risk-stratified treatment for multiple myeloma.
- The **cost** of MMprofiler is £2,800 per person (excluding VAT) in addition to standard care.

The technology

MMprofiler (Everything Genetic Ltd) is a prognostic test that uses a sample of a person's bone marrow to determine the risk of disease progression for people with multiple myeloma (newly diagnosed, relapsed or refractory). It uses the bone marrow sample for gene expression profiling of 92 genes.

Bone marrow aspiration is usually done for suspected multiple myeloma. If confirmed, MMprofiler can be used to calculate the person's SKY92 risk score, which is presented as a binary read-out (SKY92 high-risk present or absent). These results should be reviewed with standard care markers to inform healthcare professionals and people with multiple myeloma about the aggressiveness of the disease. The company claims MMprofiler will help healthcare professionals and people with multiple myeloma to choose the optimum combination of treatments.

Innovations

MMprofiler is reportedly one of the only gene expression profile tests to be developed into a validated clinical test (Shah et al. 2020). The company claims that MMprofiler is the only available technology with a CE-IVD approval for which a significant improvement in risk prediction has been shown compared with standard risk prediction in multiple myeloma.

Current care pathway

Diagnostic testing for multiple myeloma includes a bone marrow aspirate and trephine biopsy with plasma cell phenotyping, and serum protein electrophoresis and serum-free light chain assay. If serum protein electrophoresis is abnormal, serum immunofixation may

be used.

Prognostic tests use the same sample provided for diagnostic testing so people only need to have 1 bone marrow aspirate and trephine biopsy. Current prognostic testing for multiple myeloma includes the International Staging System (ISS), a 3-stage risk classification determined by the serum concentration of beta-2 microglobulin and albumin. Additionally, fluorescence in-situ hybridisation (FISH) on CD138-selected bone marrow plasma cells may be done to identify the adverse risk abnormalities t(4;14), t(14;16), 1q gain, del(1p) and del(17p)(TP53 deletion). These abnormalities, together with ISS scores, can be used to identify people with high-risk multiple myeloma.

The following publications have been identified as relevant to this care pathway:

- NICE's guideline on myeloma: diagnosis and management
- Guidelines on the diagnosis, investigation and initial treatment of myeloma: a British Society for Haematology/UK Myeloma Forum Guideline.

Population, setting and intended user

People with suspected multiple myeloma are referred to secondary care to see a haematologist for further tests. In England, genomic testing is commissioned through the NHS Genomic Medicine Service. The company has applied for MMprofiler to be added to the National Genomic Test Directory. The company states that the clinical implication for treatment based on the SKY92 result is at the discretion of the healthcare professional and person with multiple myeloma.

Costs

Technology costs

MMprofiler costs £2,800 per person (excluding VAT). Costs include logistical courier costs to the lab, analysis, and reporting. The company claims it will offer ongoing technical and clinical training as well as customer service support at no additional cost. Costs do not include bone marrow aspirate sampling which is to be done by the healthcare professional.

Costs of standard care

MMprofiler should be used with standard care markers. Costs of diagnostic bone marrow extraction average £564 per unit and range from £249 to £9,666 per unit based on 2020/21 hospital resource group (HRG) tariffs and 2019/20 national schedule of reference costs. The company states the FISH/RISS multiple myeloma panel costs about £550 per test based on information from NHS lab partners.

Resource consequences

MMprofiler has been launched in the UK. It is currently used in the private healthcare sector and in research trials within the NHS.

The company claims that using standardised and reliable prognostic risk markers like MMprofiler can play a role in ensuring the efficient use of healthcare resources. Treatment for multiple myeloma can be complex. There are several drug treatment combinations available with varied treatment intensities and related toxicities. Knowledge of a person's risk of disease progression may therefore help healthcare professionals and people with multiple myeloma in making more informed treatment decisions.

Risk-stratified treatment aims to offer people the appropriate level and combination of treatments to meet their clinical needs. The company suggests this will have several benefits. People with high-risk multiple myeloma may be spared potentially toxic treatment for which the risks outweigh the benefits. There may also be cost savings as people with standard-risk multiple myeloma could have less costly drug treatment regimens than people with high-risk multiple myeloma (Gaultney et al. 2018). Lower toxicities associated with drug treatment combinations for standard-risk multiple myeloma could also result in cost savings because of the lower incidence and treatment of peripheral neuropathy. For people who choose to have treatment, a more aggressive treatment combination can be offered, with higher level of surveillance to improve outcomes. Healthcare teams could allocate resources to people with the highest clinical need, while providing individualised care and support to all.

The company did not foresee any practical challenges associated with adopting MMprofiler. Bone marrow aspirate samples are currently sent by a next day medical express service to a lab in the Netherlands for analysis. The company states there are plans to set up a UK-based end-to-end service with United Kingdom Accreditation Service (UKAS)-accredited labs in the next 6 months. A company-led taskforce with experts in the

UK has been established to identify challenges and gaps in realising a patient-centred MMprofiler service.

Regulatory information

MMprofiler is a CE-marked IVD (IVDD Annex II List A) in vitro diagnostic device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

MMprofiler is intended for prognostic testing for all people with newly diagnosed, relapsed or refractory multiple myeloma. Multiple myeloma is more common in men: 57% of cases in the UK are in men and 43% are in women. It affects mainly people over 60 and is rare in people under 40. Most cases are diagnosed around 70 years, and the incidence rates in the UK are highest in people aged 85 to 89. Incidence rates for multiple myeloma are predicted to rise by 11% in the UK between 2014 and 2035. Multiple myeloma is around twice as common in black populations than in white and Asian populations. Incidence rates in England were similar across the most deprived quintile compared with the least. Age, sex, race, and disability are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement for medtech innovation briefings. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

There are 6 studies summarised in this briefing, including a total of 5,532 people.

The evidence includes 3 secondary analyses, of which 2 were derived from randomised

controlled trials; 1 analytical validation; 1 prospective case series; and 1 prospective single arm phase 2 trial. The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

There are 3 published secondary analyses that are not presented below (van Beers et al. [2017], Chng et al. [2016]; Kuiper et al. [2012]). These studies showed that SKY92 (formerly known as EMC92) performed well compared with other gene expression classifiers and showed improved performance when combined with other gene expression profile signatures. Kuiper et al. (2012) also outlines the development of the SKY92 (EMC92) gene expression signature.

Overall assessment of the evidence

The evidence for MMprofiler is of moderate quality. Most studies evaluated the clinical or analytical validity of the technology, with 3 studies comparing the technology with other prognostic markers. Studies showed consistent findings supporting the performance of MMprofiler (known as EMC92 or SKY92 in clinical research) in isolation or when combined with other markers. The predominance of secondary analyses meant the methodological information included in these papers were limited in detail compared with primary studies. Two studies examined differential treatment effects based on people's risk classification while 1 study explored the impact of SKY92 risk scores on treatment decisions. One study examined response rates to an intensive treatment strategy in people with ultrahigh-risk multiple myeloma determined by genetic screening, including SKY92. These studies show that SKY92 risk classification can potentially affect treatment decisions and outcomes. Further evidence is needed evaluating the use of MMprofiler in treatment decisions and its effect on clinical outcomes compared with standard care markers. Further prospective comparative research is also needed on risk-stratified treatment for multiple myeloma in clinical practice.

Biran et al. (2021)

Study size, design and location

Prospective case series of 147 people with multiple myeloma enrolled from 5 centres in the US. This paper reports initial findings from the ongoing PROMMIS trial.

Intervention and comparator

MMProfiler SKY92 compared with routine clinical practice.

Key outcomes

This study describes the clinical relevance of MMprofiler in helping healthcare professionals with treatment decisions. MMprofiler classified 43 out of 147 (29%) people as having SKY92 high-risk. The risk distribution by R-ISS (revised International Stating System [ISS]) was 33% (44/133) stage 1, 58% (77/133) stage 2, and 9% (12/133) stage 3. Before knowing SKY92 risk classification, healthcare professionals classified 73 (50%) people as having high-risk multiple myeloma, 46 of whom were classified by MMprofiler as having SKY92 standard-risk. Review of SKY92 risk scores in these cases resulted in healthcare professionals reclassifying 30 people as having standard-risk multiple myeloma. For the 74 people initially regarded by healthcare professionals as having standard-risk multiple myeloma, MMprofiler identified 16 as having SKY92 high-risk. After reviewing the SKY92 risk scores, healthcare professionals agreed with reclassification in all cases. For 131 (89%) people, the final risk classification assigned by healthcare professionals matched the SKY92 result. Changes in risk classification affected proposed treatment plans, especially options after autologous stem cell transplant. Treatment plans were de-escalated in the 30 people reclassified as having standard-risk multiple myeloma and escalated in 15 of the 16 people reclassified as having high-risk multiple myeloma. Healthcare professionals also found SKY92 scores helpful in confirming risk classifications and treatment plans in concordant cases. MMprofiler affected treatment decisions in 37% (54/147) of cases, which was above the predefined threshold of clinical relevance of 15% ($p<0.001$). SKY92 results also reportedly increased healthcare professionals' confidence in their proposed treatment plan.

Strengths and limitations

This study is a prospective multicentre study comparing MMprofiler with routine clinical practice used by 30 healthcare professionals (haemato-oncologists). Routine clinical practice was not defined and therefore the risk classification methods used may have varied across healthcare professionals and centres. Healthcare professionals were blinded to MMprofiler results for their initial risk assessment and treatment planning. Authors suggested there may have been some recruitment bias because the number of people classed as having high-risk multiple myeloma in the cohort (29%) was higher than reported in the literature (15% to 25%). It is possible that healthcare professionals selected

people with perceived higher risk multiple myeloma to be included in the study. The study initially recruited 250 people but 103 were excluded because of screen failure including smouldering (not active) multiple myeloma or low-quality bone marrow sample. The PROMMIS study was sponsored by SkylineDx (the company behind MMprofiler) and several members of the research team disclosed employment with or financial interest in the company.

Kaiser et al. (2021) [abstract]

Study size, design and location

Prospective single arm phase 2 trial of 107 people with ultrahigh-risk, newly diagnosed multiple myeloma or plasma cell leukaemia recruited from 39 hospitals in the UK. This abstract reports initial findings from the UK optimum/MUKnine trial which aimed to determine if a novel treatment combination was sufficiently active to take forward to a phase 3 trial.

Intervention

People with ultrahigh-risk, newly diagnosed multiple myeloma (detected by central trial genetic or SKY92) or plasma cell leukaemia had up to 6 cycles of daratumumab, cyclophosphamide, bortezomib, lenalidomide, dexamethasone (Dara-CVRd) induction, augmented high-dose melphalan, and autologous stem cell transplantation augmented with bortezomib, followed by Dara-CVRd consolidation for 18 cycles and daratumumab with lenalidomide (Dara-R) maintenance.

Key outcomes

Median follow up was 22.2 months (95% confidence interval 20.6 to 23.9). Two people died during induction because of infection. Responses in the intention-to-treat population at the end of induction were 94% overall response rate with 22% complete response, 58% very good partial response, 15% partial response, 1% progressive disease, and 5% timepoint not reached. Reponses at day 100 after autologous stem cell transplant were 83% overall response rate with 47% complete response, 32% very good partial response, 5% partial response, 7% progressive disease, and 10% timepoint not reached. Minimal residual disease status after induction was 41% minimal residual disease negative, 40% minimal residual disease positive, and 19% not evaluable. Minimal residual disease status at day 100 after autologous stem cell transplant was 64% minimal residual disease

negative, 14% minimal residual disease positive, and 22% not evaluable. Authors concluded that response rates were high, with toxicity comparable to other induction regimens.

Strengths and limitations

This study seems to be the first to use genetic screening including SKY92 to prospectively identify people with ultrahigh-risk, newly diagnosed multiple myeloma to be offered an intensive treatment schedule. Ultrahigh-risk, newly diagnosed multiple myeloma is rare, occurring in about 20% of people with multiple myeloma. Recruitment of people from this patient group was achieved through multicentre involvement across 39 hospitals in the UK. The study reports high response rates in treating this difficult-to-treat population with the intensive treatment strategy. This provides some early support for the idea of risk-stratified treatment in multiple myeloma and highlights the need for further comparative research in this area. This study was reported in abstract and was therefore limited in detail.

van Beers et al. (2021)

Study size, design and location

Analytical validation of SKY92 assay on bone marrow samples from 12 people with multiple myeloma and 7 reference cell line samples.

Intervention and comparator

SKY92 gene assay; no comparator.

Key outcomes

SKY92 was found to be an appropriately sensitive test, producing robust results with varied levels of RNA input in line with the recommended minimum tumour content for the assay. The SKY92 result was not affected by the presence of interfering substances with the test demonstrating specificity in detecting high-risk multiple myeloma. The test also showed good repeatability and intermediate precision when analysed for the effect of differing reagents, microarrays, instruments, and operators. None of the precision tests done exceeded the maximum allowed standard deviation of 0.45, with class switching because of imprecision below 10%. The SKY92 array showed high reproducibility in clinical

samples across 3 independent labs. Based on these findings, the SKY92 assay was said to meet or exceed the requirement for a prognostic test used in routine clinical practice.

Strengths and limitations

This study provides analytical validation of the procedural parameters to run the MMprofiler SKY92 assay in clinical settings. Analysis was guided by relevant Clinical and Laboratory Standards Institute standards and pre-defined statistical acceptance criteria. Several members of the research team disclosed employment with or financial interest in SkylineDx.

Shah et al. (2020)

Study size, design and location

Secondary analysis of 329 people with newly diagnosed multiple myeloma enrolled in a multicentre randomised controlled trial in the UK.

Intervention and comparator

SKY92 gene signature compared with chromosomal aberrations assessed using quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) and multiplex ligation-dependent probe amplification.

Key outcomes

SKY92 identified 81 of 329 (24.6%) people as having SKY92 high-risk. People classed with SKY92 high-risk had shorter progression-free survival (median 16.0 months compared with 33.8 months; $p<0.001$) and overall survival (median 36.7 months compared with not reached; $p<0.001$). SKY92 and chromosomal high-risk markers were combined to produce 4 risk groups: SKY92 and double-hit chromosomal high-risk markers (9.7%), SKY92 or double-hit chromosomal high-risk markers (23.4%), single chromosomal high-risk marker (24%), and no risk marker (42.9%). Progression-free survival and overall survival rates showed significant improvement across higher to lower risk groups. Differential treatment effects were found for the different risk groups. Lenalidomide single-agent maintenance extended progression-free survival in people with the single chromosomal high-risk marker or no risk marker when compared with observation. This benefit was not seen in people with SKY92 or double-hit chromosomal high-risk markers.

Strengths and limitations

This study provides clinical validation of the MMprofiler SKY92 gene signature and shows its independent prognostic prediction when compared with chromosomal high-risk markers. It shows the utility of combining MMprofiler with chromosomal markers to detect high-risk multiple myeloma. Some evidence was provided to suggest benefit in using prognostic markers in treatment decision making.

Kuiper et al. (2020)

Study size, design and location

Secondary analysis of 180 people with previously untreated symptomatic multiple myeloma enrolled in a randomised controlled trial in the Netherlands, Denmark, Sweden and Norway. The larger trial (n=636) compared treatment with melphalanprednisone-thalidomide followed by thalidomide maintenance (MPT-T) to melphalan-prednisone-lenalidomide followed by lenalidomide maintenance (MPR-R).

Intervention and comparator

SKY92 gene classifier compared with SKY-RISS (SKY92 combined with revised ISS [R-ISS]).

Key outcomes

Combining SKY92 with R-ISS (n=168) resulted in 3 risk groups: low-risk (SKY-RISS 1; 15%), intermediate-risk (SKY-RISS 2; 74%), and high-risk (SKY-RISS 3; 11%). The 3-year progression-free survival rates for these groups were 54%, 27% and 7%, respectively ($p<0.001$). The respective 3-year overall survival rates were 88%, 66% and 26% ($p<0.001$). SKY-RISS was independent of other prognostic markers for progression-free survival and overall survival. A differential treatment effect was seen in the SKY-RISS 3 group (n=18), with MPR-R treatment resulting in longer overall survival compared with MPT-T (57% compared with 0%; median overall survival 55 months compared with 14 months; $p=0.007$). No difference in overall survival was found between treatment arms for SKY-RISS 1 (n=124) or SKY-RISS 2 (n=26). These treatment effects were also seen in the R-ISS 3 and SKY92 high-risk groups but were less pronounced. Combining SKY92 with R-ISS resulted in more accurate risk classification compared with either individual prognostic marker.

Strengths and limitations

This study validates the use of the MMprofiler SKY92 gene classifier to predict progression-free survival and overall survival in multiple myeloma. The findings suggest a benefit of using SKY-RISS as a prognostic test to assist in treatment decisions for people with high-risk multiple myeloma. The study was a secondary analysis with a small number of people classified as having high-risk multiple myeloma in the treatment arms.

Kuiper et al. (2015)

Study size, design and location

Secondary analysis of 4,750 people with myeloma from multiple independent data sets.

Intervention and comparators

EMC92 compared with 7 gene expression classifiers (UAMS17, UAMS70, UAMS80, IFM15, MRCIX6, HM19, and GP150) and standard prognostic markers (ISS, fluorescence in-situ hybridisation [FISH]).

Key outcomes

Gene expression classifiers appeared to show better risk separation than ISS and FISH. The percentage of high-risk classifications varied between gene expression classifiers, with EMC92 identifying more people with high-risk multiple myeloma (18%) than the other classifiers (8% to 12%). The EMC92-ISS compound risk marker had the best median rank score when ranked on performance against all single and combined risk markers. EMC92 was the best single marker (ranked 7th out the 32 markers), while ISS was ranked 23rd. EMC92-ISS classifies people into 4 risk groups: low risk (38%; median overall survival not reached after 96 months), intermediate to low risk (24%; median overall survival 61 months), intermediate to high risk (22%; median overall survival 47 months), and high risk (17%; median overall survival 24 months). EMC92-ISS showed utility in identifying both high- and low-risk multiple myeloma. This was described as an advantage over FISH markers which identified only high risk.

Strengths and limitations

This study suggests MMprofiler combined with ISS is a strong prognostic marker for

multiple myeloma. Analysis included multiple independent data sets resulting in the validation of findings in a large sample of people with multiple myeloma. However, the secondary analysis of these data sets limits details of the methodology and quality of the primary studies.

Sustainability

MMprofiler is a single-use prognostic test. The company claims the technology will have lower environmental affect compared with current UK practice. There is no published evidence to support these claims.

Recent and ongoing studies

- MUK Nine b: OPTIMUM: A phase 2 trial evaluating novel combination of biological therapy in people with high-risk multiple myeloma. ClinicalTrials.gov identifier: NCT03188172. Status: recruiting. Indication: multiple myeloma. Last updated: April 2019. Country: UK.
- PRospective Multiple Myeloma Impact Study (PROMMIS): A prospective, case series to measure the impact of MMprofiler on treatment intention decisions in multiple myeloma. ClinicalTrials.gov identifier: NCT02911571. Status: recruiting. Indication: multiple myeloma. Devices: MMprofiler SKY92 gene signature. Last updated: October 2020. Country: the US.
- Validation of a Personalised Medicine Tool for Multiple Myeloma That Predicts Treatment Effectiveness in Patients (MMpredict). ClinicalTrials.gov identifier: NCT03409692. Status: active, not recruiting. Indication: multiple myeloma. Devices: MMprofiler. Last updated: April 2021. Country: Italy.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 5 experts were familiar with MMprofiler, with 4 experts involved in clinical or bibliographic research on the technology or procedure.

Level of innovation

All experts said MMprofiler is innovative, with 4 stating it is the first in a new class of testing. Four experts said MMprofiler finds prognostic information that is not currently found by other methods including FISH. One expert stated that FISH also finds prognostic information not found by MMprofiler, with MMprofiler plus FISH used to identify people with ultrahigh-risk multiple myeloma. One expert felt that while MMprofiler is innovative, it has not been shown to be better than standard care in terms of risk classification in multiple myeloma. Two experts described other gene expression profiling platforms but stated these were not equivalent to MMprofiler.

Potential patient impact

All experts stated MMprofiler may detect people with high-risk multiple myeloma not identified by other prognostic tests. One expert said routinely used prognostic markers are effective at risk-stratification and felt more direct comparative evidence was needed to show that MMprofiler was better. Three experts felt MMprofiler could improve people's knowledge and understanding of the prognosis of their cancer. This could improve communication between patients, healthcare professionals and carers leading to more empowerment of people in their treatment decisions and care plans. One expert stated that having better prognostic information may also help people with life plans, such as stopping work and financial planning. However, they questioned how much this additional prognostic information would affect people's decision making.

One expert felt MMprofiler has the potential to guide treatment in the future based on genetic risk scores. Two experts stated there is no evidence that the technology is a predictive biomarker. Predictive information would estimate differential responses to treatments and guide treatment decisions. All experts noted that healthcare professionals are still unsure how to manage multiple myeloma according to risk classification. They felt more research and data were needed to support the use of risk-stratified treatment for multiple myeloma. One expert noted that while the benefits of risk-stratified treatment are still unclear, most multiple myeloma experts believe that people with high-risk multiple myeloma should be treated differently.

There were few anticipated adverse events from using MMprofiler. One expert said there may be low false positive or false negative rates which may lead to the wrong risk classification in some people. They felt it was hard to estimate the potential effect of this. One expert felt that inappropriate treatment decisions could be made if the technology

was used for risk-stratified treatment before evidence supporting this is mature.

Potential system impact

All experts stated that MMprofiler is not currently used in the NHS. One expert believed MMprofiler has the potential to change the current pathway by better defining genetic risk. This would allow for individualised treatment approaches like other cancers. One expert stated the improved prognostic information from combining MMprofiler with standard care prognostic tests could lead to improved allocation of resources through risk adapted management pathways. Three experts felt more data was needed to show the capability of MMprofiler to influence treatment decisions. One expert stated that while MMprofiler may have better prognostic power than standard care, they were unsure this was significantly better to justify its use without having predictive data. They added that if the technology could provide predictive information in the future, it could be adopted quickly and either replace or supplement current cytogenetic tests.

Four experts stated MMprofiler costs more than standard care. One expert believed the technology would be cost neutral when balancing test costs against the improved allocation of resources in the patient management pathway. One expert stated that while prognostic tests were being used to identify high-risk multiple myeloma, this did not result in any healthcare resource utilisation savings. Two experts stated there would be minimal resource needs because the test is done by the company on existing bone marrow samples. One expert queried the quality assurance of sample turnaround and processing of tests done at a laboratory outside of the UK. All agreed there would be no need for specific training for efficacious and safe use.

General comments

There was disagreement over where the technology would be used in the NHS. Two experts felt this would be limited to a small number of hospitals or specialist centres, while 3 experts thought it would be used by most or all district general hospitals. Four experts believed the technology could be offered to all people with newly diagnosed multiple myeloma. There are about 5,800 new diagnoses of multiple myeloma in the UK every year. The test could also be offered to more than half of people with relapsed multiple myeloma. One expert suggested use may be limited to certain groups whose treatment decisions may be more affected by genetic disease risk. These included older people and people with patient-specific factors such as frailty and comorbidities. One expert suggested use

may be most relevant in younger people as the prognostic effect of tumour genetic lesions is greater in this group.

Two experts stated that it was unlikely that the technology would be universally adopted. The main factors thought to limit adoption in the NHS were the lack of mature evidence, costs, and variable uptake by healthcare professionals. All experts said further prospective research of the technology and its predictive capacity in guiding treatment decisions was needed.

Expert commentators

The following clinicians contributed to this briefing:

- Dr Christopher Parrish, consultant haematologist, Leeds Teaching Hospitals NHS Trust. Participated in advisory board for Everything Genetic Ltd.
- Prof Gordon Cook, professor of haematology and clinical director of National Institute for Health Research (NIHR) Leeds Medtech and In Vitro Diagnostics Cooperative, University of Leeds. Did not declare any interests.
- Prof Guy Pratt, consultant haematologist, University Hospitals Birmingham. Participated in advisory board for Everything Genetic Ltd.
- Dr Martin Kaiser, research team leader and consultant haematologist, Royal Marsden Hospital and the Institute of Cancer Research, London, UK. Has provided unpaid technical advice for SkylineDx in relation to SKY92 as part of research performed in the OPTIMUM/MUKnine trial.
- Dr Kevin Boyd, consultant haemato-oncologist, The Royal Marsden NHS Foundation Trust. Did not declare any interests.

Development of this briefing

This briefing was developed by NICE. NICE's interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

ISBN: 978-1-4731-4216-9