



Bone marrow tests

Myeloma cells grow in the bone marrow, and the only way to assess their properties is to remove a sample of these cells and to analyze them. Some of these tests can be done by a pathologist looking through a microscope and others require sophisticated computers with customized software programs.

Bone marrow biopsies aim to assess the following:

- many myeloma cells there are,
- what they look like as compared to normal plasma cells,
- what their cellular genetics are,
- how rapidly they're reproducing, and
- which type of antibodies they express.



When Are Bone Marrow Aspiration and Bone Marrow Biopsy Used in Myeloma?

Bone marrow aspiration and bone marrow biopsy are routinely performed at diagnosis. They are also ordered at the doctor's discretion at the following junctures:

- annually during a period of remission
- when the doctor deems it necessary to determine a patient's status

Bone marrow biopsy is also a reliable way to monitor the status of patients with oligosecretory or non-secretory myeloma; also, Serum Free Light Chain (sFLC) can be used in a number of such cases.

What Makes Up a Person's Bone Marrow?

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WITHDRAW CONSENT

How Are Bone Marrow Exams Performed?

A complete bone marrow exam requires both an aspirate of the liquid portion of the marrow and a core specimen of the solid portion, which includes a piece of the bone tissue with its enclosed marrow. To make the process less uncomfortable, bone marrow aspiration and biopsy should be performed by experienced technicians using anesthetics and improved needles.

Understanding the Results of Bone Marrow Biopsies in Myeloma

Plasma cell percentage

The normal range is 1%–2% (Note: < 5% is complete response, or CR).

The pathologist will examine the bone marrow aspirate or core under the microscope and determine the percentage of plasma cells in the sample:



Normal bone marrow has about 2% or fewer plasma cells.

The presence of 60% or more plasma cells in the bone marrow is an independent myeloma-defining event.

Myeloma cells aren't distributed evenly throughout the bone marrow in the skeleton. For that reason, the iliac crest is most often chosen as the biopsy site. It provides the best representative sample.

Plasma cell morphology

The appearance of myeloma cells is distinct, with large nuclei that make the cells look like pimento-stuffed olives. The pathologist records the appearance and number of these cells. Words such as "mature," "immature," or "atypical" are used to describe the plasma cells. Generally, "mature" cells suggest a better prognosis than "immature" or "atypical" plasma cells.

Specimen quality

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renewing assessments.

Immunohistochemistry (also known as Immunophenotyping) and Flow Cytometry

Immunohistochemistry (IHC), also called immunophenotyping, is the process of detecting antigens in tissue samples by introducing antibodies that bind to them.

IHC is one of the tests used to determine stringent complete response (sCR) to therapy as defined by the [IMWG Uniform Response Criteria](#) ([/resource-library/international-myeloma-working-group-imwg-uniform-response-criteria-multiple](#)) . In addition to the criteria for complete response (CR), the IMWG criteria for sCR include a normal free light chain ratio and the absence of clonal plasma cells in the bone marrow by immunohistochemistry or immunofluorescence.



Immunophenotypic analysis of a myeloma patient's bone marrow identifies myeloma protein markers, if they are present. A fluorophore, or fluorescent marker, is attached to each antibody. It glows when it finds the correct antigen on the surface of the myeloma cells. Several antibodies are usually used simultaneously. The fluorophores are given different colors (fluorochrome) for each antibody. The bone marrow sample cells and selected antibodies are sent through a flow cytometer.

A flow cytometer is a laser-based instrument that reads the fluorophores and identifies and sorts the myeloma cells.

Next Generation Flow (NGF) cytometry is

- a highly accurate way to detect minimal residual disease (MRD) after treatment

- uses many antibodies and myeloma-specific computer software to rapidly perform eight-color immunophenotyping of myeloma cells

- can detect 1 myeloma cell per approximately 1,000,000 bone marrow a laboratory sample

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Since the active growth rate of myeloma cells is usually fewer than 3%, this provides an incomplete assessment of chromosomal changes.

If abnormalities are noted, they are important. These abnormalities appear in the few cells that are actually growing.

When can cytogenetic testing be performed?

This test may be performed on the bone marrow of newly diagnosed myeloma patients.

It can be performed again after treatment to see if the therapy has eliminated all the cells with chromosomal abnormalities.

It may also be performed at relapse to help determine

if it is time to resume therapy, and

if one therapy might be preferable to another.



In the laboratory, after the bone marrow specimen is allowed to grow in a special dish, the cells are stained and photographed to provide a karyotype that shows the number and arrangement of the chromosomes.

The chromosomes can be karyotyped only if the cells are undergoing division. Karyotyping is particularly valuable for

identifying higher-than average-risk myeloma in patients with fewer than two copies of each chromosome (hypodiploidy)

in those whose 13th chromosome is partially deleted during cell division (called "del 13" or "13q-").

Fluorescence In-Situ Hybridization (FISH)

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marrow sample.

It allows detection of changes whether myeloma cells are growing or not.

It can detect numerical and structural chromosomal abnormalities.

For FISH:

1. The cells are fixed in paraffin wax.
2. Fluorescent probes that bind to certain sequences of the chromosome are attached.
3. Finally, each chromosome can be identified by a different color.



Chromosomes are made up of two chromatids paired in an X form, with the X shorter at the top and longer on the bottom. The "short arms" at the top half of the X are labeled "p" and the "long arms" at the bottom are labeled "q." During normal cell division, the chromosomes divide in two, each single chromatid forming a duplicate of its genetic material in a new cell.

FISH is capable of detecting chromosomal translocations that can occur when gene sequences of one chromatid get shifted over to another chromatid during cell division, and the colors of the fluorescent probes from one chromosome appear in a different chromosome. Chromosomal deletions can be detected when a fluorophore color is absent.

What do FISH test results determine?

FISH results have been incorporated into the revised International Staging System (R-ISS) (/international-staging-system-iss-revised-iss-r-iss) for myeloma because they provide a powerful tool for predicting risk and survival in myeloma.

The following cytogenetic abnormalities are considered to show high risk:

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Watch [this Ask Dr. Durie video \(/node/8294\)](/node/8294) to learn more.

1q+ (gain of an additional long arm on chromosome 1) Watch [this Ask Dr. Durie video \(/node/8294\)](/node/8294) to learn more.

Some chromosomal abnormalities signal aggressive myeloma. Other such abnormalities have no negative prognostic impact.

Nearly all myeloma patients demonstrate deletion of all or parts of chromosome 13 by FISH analysis. This is why deletion 13 is better determined by standard cytogenetics than by FISH.

How are therapy choices related to chromosomal status?



The loss of the short arm of chromosome 17 by FISH analysis shows especially high risk because of an important tumor suppressor gene, p53, is located there. Tumor suppressor genes, also known as **anti-oncogenes**, control cell division and help prevent cancer cells from developing.

Therapy choices are often related to chromosomal status. For example:

Regimens with [Velcade® \(bortezomib\) \(/velcade-bortezomib\)](/velcade-bortezomib) for induction and maintenance therapy are preferred for patients with t(4;14) myeloma.

[Pomalyst® \(pomalidomide\) \(/pomalyst-pomalidomide\)](/pomalyst-pomalidomide) is less effective than Velcade for t(4;14),

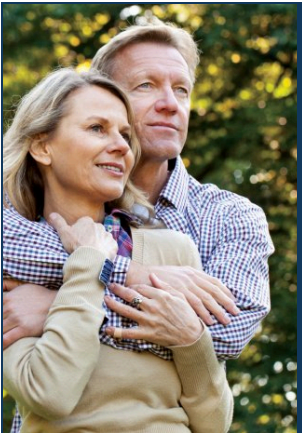
Yet, in studies thus far, Pomalyst is more effective than Velcade for overcoming the negative impact of del 17p.

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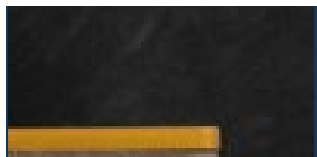
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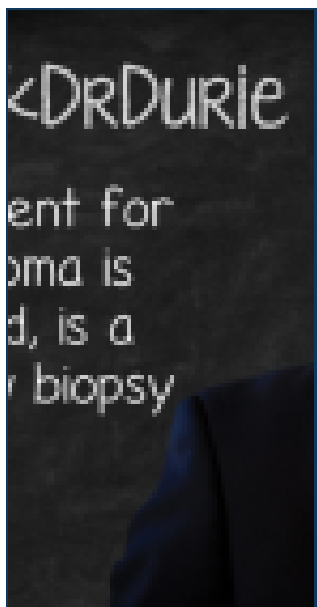
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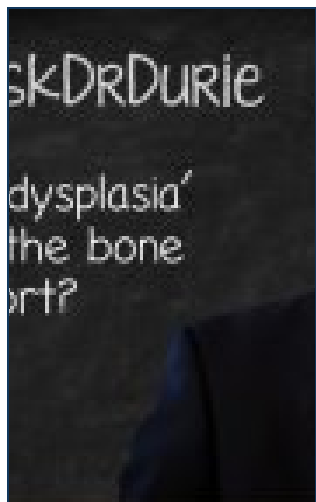
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