MULTIPLE MYELOMA
Frequently Asked Questions?

MULTIPLE MYELOMA PRECURSOR CONDITIONS

How are patients with smoldering multiple myeloma (SMM) managed?
According to treatment guidelines, patients with a multiple myeloma precursor condition such as SMM are typically not treated. Instead, they are followed closely by a doctor, who looks for changes that indicate a progression to myeloma. Some patients with SMM have a higher risk of developing myeloma; several clinical trials are currently examining whether there is any benefit to treating higher-risk SMM patients to see if treatment prevents or delays the development of multiple myeloma. SMM patients with high-risk features should discuss with their care team whether participation in a clinical trial is appropriate for them.

Are patients with SMM at higher risk for developing multiple myeloma?
Because not all SMM is the same, doctors gauge each SMM patient's risk of developing multiple myeloma. A myeloma specialist will often use a risk-stratification tool called the 2/20/20 model, which uses blood and bone marrow biopsy test results that include serum M protein levels over 2 g/dL, serum free light-chain ratio levels over 20, and more than 20% bone marrow plasma cells. SMM patients with two or more of these values are considered high risk and have a 50% risk of developing multiple myeloma within 2 years after diagnosis. The likelihood for an SMM patient developing multiple myeloma is 10% per year for the first 5 years.

The 2/20/20 model does not report the presence of chromosomal abnormalities in the bone marrow sample. Chromosomal abnormalities do, however, influence a patient's risk of developing myeloma. To determine whether any chromosomal abnormalities are present, the doctor will order genetic tests, which help provide a full picture of an SMM patient's risk for developing multiple myeloma.

What factors increase the risk of developing myeloma for patients with SMM?
All individuals have two pairs of 23 chromosomes (one set from each parent). A number of abnormalities can affect chromosomes, including the loss of a piece (deletion), the swapping of pieces between chromosomes (translocation), the absence of one chromosome from a pair (monosomy), or the presence of an extra copy (trisomy). Several abnormalities increase the risk of developing myeloma—it is these abnormalities that genetic tests look for.

Each chromosome pair is given a number or letter designation. Each chromosome has a long arm—called q—and a short arm—called p. If, for example, a patient is said to have a deletion 17p (also sometimes written as del17p), that means that the patient has a deletion (a part of the chromosome is missing) within the short arm of chromosome 17. Another genetic change that can happen is chromosomal translocation. Translocation occurs when part of one chromosome breaks off and switches places with part of another chromosome. If, for example, a patient is said to have a translocation between chromosome 4 and chromosome 14 (abbreviated t[4;14]), this means that part of chromosome 4 broke off and switched places

with part of chromosome 14. Another abnormality that can occur is when a person has something other than two copies of a chromosome. This can include only one copy (monosomy), three copies (trisomy), or even more copies and is sometimes written as + (for example, +1q designates additional copies of the long arm of chromosome 1). For SMM, high-risk chromosomal abnormalities include t(4;14), t(14;16), del17p, +1q, and del13q/monosomy 13.

Doctors may repeat the genetic analysis if a patient is higher risk or the patient's clinical presentation changes and/or may recommend testing yearly or every other year to look for any changes.

What questions should patients with SMM or monoclonal gammopathy of undetermined significance (MGUS) ask their community oncologist or primary care provider regarding participation in a clinical trial?

There are many clinical trials under way for patients with MGUS or SMM, including studies investigating the factors that may predict a patient's risk of progressing to multiple myeloma.

For SMM patients at highest risk of developing multiple myeloma, trials are available that are investigating the use of different multiple myeloma treatments to prevent the development of multiple myeloma.

Patients with MGUS or SMM should discuss with their care team whether participation in a clinical trial is appropriate for them.

Patients with MGUS or SMM should ask their doctor:

- What is my risk of developing multiple myeloma?
- What clinical trials are available to someone with my risk profile?
- What are the benefits and risks of participating in a clinical trial?
- What are my options if I do not participate in a clinical trial?