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Continuing Medical Education (CME) Questions

IgM-MM is a pre–germinal center MM

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Bazarbachi AH, Avet-Loiseau H, Szalat R, Samur AA, Hunter Z, Shammas M, Corre J, Fulciniti M, Anderson KC, Parmigiani G, Treon SP, Mohty M, Munshi NC, Samur MK. IgM-MM is predominantly a pre-germinal center disorder and has a distinct genomic and transcriptomic signature from WM. *Blood*. 2021;138(20):1980-1985.

1. Your patient is a 67-year-old man with immunoglobulin M (IgM)–producing gammopathy. According to the genomic study by Bazarbachi and colleagues, which of the following statements about genomic and transcriptomic characteristics of IgM-multiple myeloma (MM) through whole-genome sequencing (WGS) and transcriptome sequencing of IgM-MM cases compared with non-IgM-MM, Waldenström macroglobulinemia (WM), and healthy donor plasma cells (PCs) is correct?

- ☐ IgM-MM showed dramatic differences from MM in its defining structural variants and gene-expression profiling
- ☐ Key features of IgM-MM were t(11;14) translocation, chromosome 6 and 13 deletion, and distinct molecular and transcription factor signatures
- ☐ IgM-MM translocations were mostly characterized by the usual class-switching region breakpoints
- ☐ WGS describes IgM-MM as predominantly a post–germinal center malignancy without molecular differences from WM

2. According to the genomic study by Bazarbachi and colleagues, which of the following statements about driver mutations in IgM-MM compared with non-IgM-MM, WM, and healthy donor PCs is correct?

- ☐ The high frequency of the clock-like signature in IgM-MM and WM vs non-IgM-MM and high APOBEC in IgM-MM vs WM suggest alternate mechanisms in these groups
- ☐ RNA-sequencing data from IgM-MM showed decreased expression of transcripts relevant to MM-associated proteins
- ☐ IgM-MM has a fully immature signature/phenotype compared with non-IgM-MM and WM
- ☐ The presence of t(11;14) and del13, coupled with the lack of *MYD88* mutation at a precursor level, may predict progression of monoclonal gammopathy of undetermined significance to WM rather than to IgM-MM

3. According to the genomic study by Bazarbachi and colleagues, which of the following statements about potential therapeutic targets in IgM-MM is correct?

- ☐ Rituximab is likely to be ineffective in patients with IgM-MM
- ☐ BTK inhibitors, such as ibrutinib, are very effective in treating MM but have only modest activity in WM and IgM-MM
- ☐ Venetoclax is more likely to be effective in non-IgM-t(11;14)-MM than in IgM-MM
- ☐ High BCL2/BCL2L1 ratio and high expression of CD20 and BTK in IgM-MM could provide potential therapeutic targets

DOI 10.1182/blood.2021014410