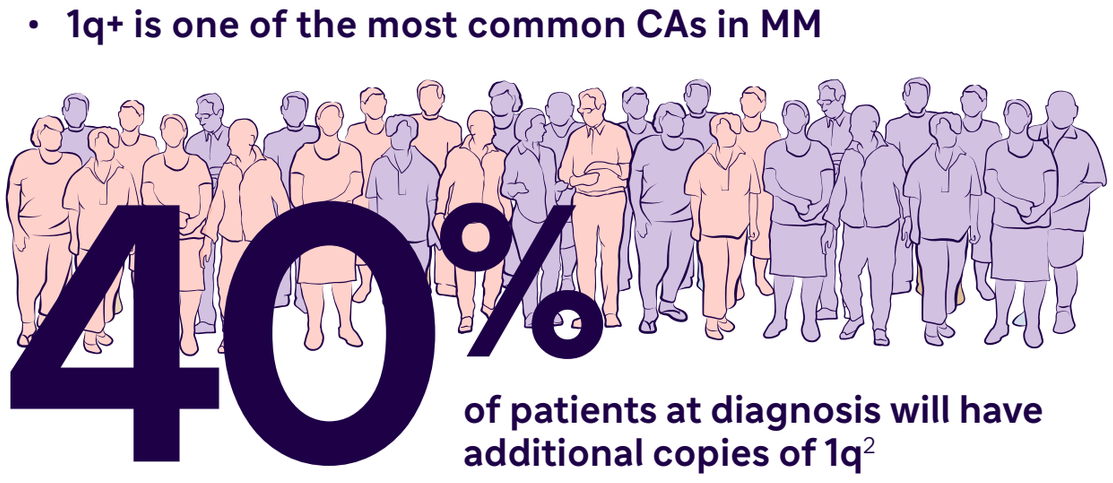
Multiple Myeloma: Chromosome 1q+ cytogenetic abnormalities

Multiple copies of chromosome 1 (1q+) is a frequent CA in MM

- MM is characterized by CAs in plasma cells[1]
- Frequent gains include 1q, 6p and 11q[1]
- 1q+ is one of the most common CAs in MM



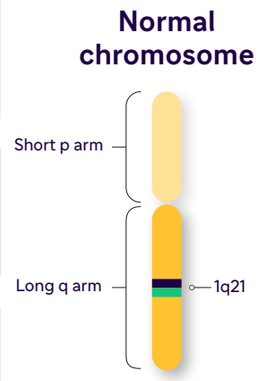
40%

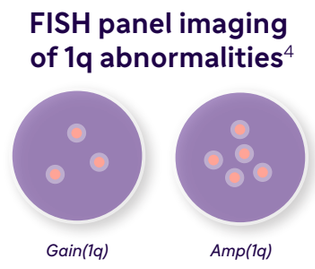
of patients at diagnosis will have additional copies of 1q[2]

1q+ abnormalities are defined by copy number

Chromosome 1q abnormalities terminology[3]

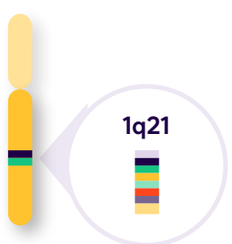
+1q	**Additional copies of any part of the long arm of chromosome 1 (1q), irrespective of copy number or DNA segment gained**
Gain(1q)	**Gain of only 1 extra copy of chromosome 1q (3 total copies)**
Amp(1q)	**"Amplification" of 1q, with ≥2 additional copies of chromosome 1q (4 or more total copies)**





In MM, 1q+ is frequently denoted as 1q21+, which refers to a specific location – region 2, band 1 on the long arm of chromosome 1

Overexpression of certain genes in the 1q arm may drive pathogenesis and drug resistance[4,5]



Key genes located in the 1q21 band:
- **BCL9:** Cell growth
- **ILF2, ADAR:** RNA metabolism
- **MCL1:** Anti-apoptosis
- **CKS1B:** Cell proliferation

- **PSMD4:** Anti-PI

Resistance to PIs through the upregulation of the proteasome genes, including PSMD4[6]

Other key genes outside of the 1q21 band include:
- **SLAMF7, SLAMF3:** Immunomodulatory receptors
- **FCRH5, NEK2:** Cell development
- **CD1D:** T-cell responses

- **CD55, CD46:** CDC inhibition

Resistance to drugs that rely mainly on CDC through upregulation of complement inhibitors, such as CD55[7]

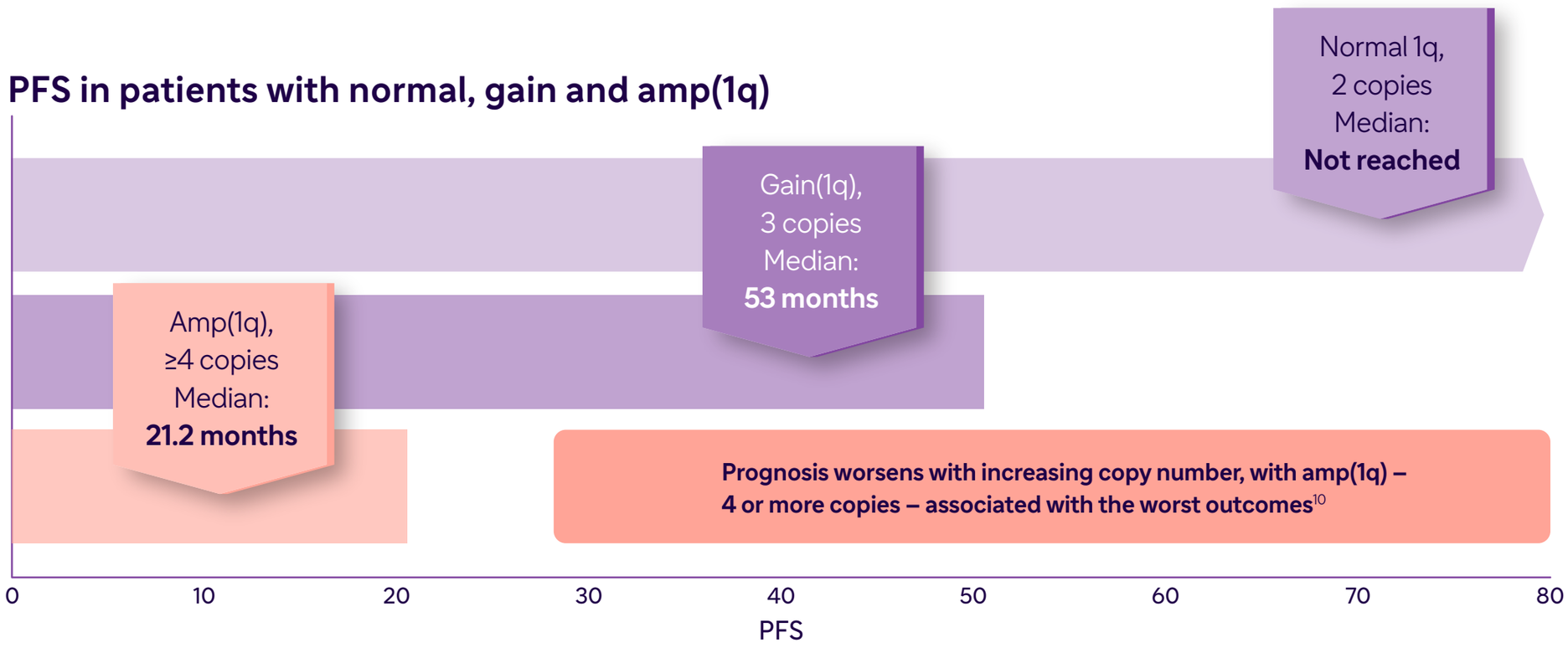
1q+ terminology when co-occurring with/without other high-risk cytogenetic abnormalities (HRCA)[8]

1q+ increases throughout the MM disease course[4,9]

Accumulation of 1q+ clones and 1q copy number

1q+ is associated with poor outcomes, especially when presenting with other CAs

PFS in patients with normal, gain and amp(1q)



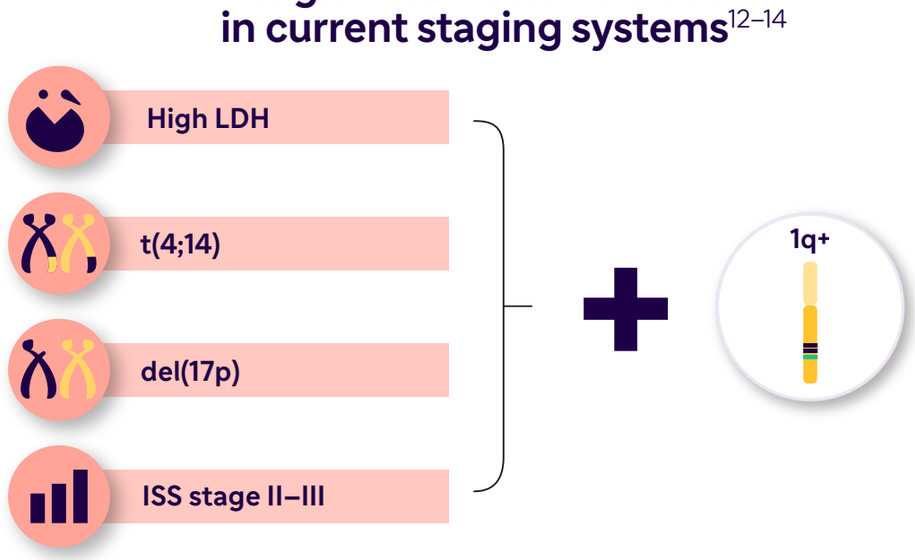
PFS and OS are significantly worse in patients with 1q+ versus patients without 1q abnormalities[10]

Co-occurrence of 1q+ with other high-risk factors has been associated with very poor prognosis (ultra-high-risk)[11,5]

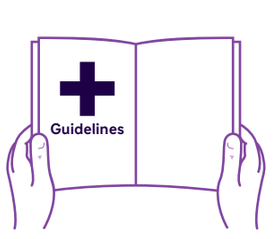
Incorporating 1q+ testing into clinical practice remains challenging

New staging systems, such as R2-ISS, MASS and R-ISS-1q,[12–14] are including gain/amp(1q), alongside other high-risk factors when defining disease stage, in order to refine predictions of clinical outcomes and highlight the prognostic impact of gain/amp(1q)

High-risk factors included in current staging systems[12–14]



Although most guidelines include 1q+ in their HRCA definitions, the recommendations for FISH panel testing for 1q+ are inconsistent and there is little treatment guidance specific to gain/amp(1q)[15–17]



IMWG guidelines include gain/amp(1q) in their definition of HRCAs, but **do not** include it as part of their recommended routine FISH panel[15]

CA, cytogenetic abnormality; **CDC**, complement-dependent cytotoxicity; **FISH**, fluorescence in situ hybridization; **HRCA**, high-risk cytogenetic abnormality; **IMWG**, International Myeloma Working Group; **ISS**, international staging system; **LDH**, lactate dehydrogenase; **MASS**, The Mayo Additive Staging System; **MM**, multiple myeloma; **MRD**, minimal residual disease; **NDMM**, newly-diagnosed multiple myeloma; **OS**, overall survival; **PFS**, progression-free survival; **PI**, protease inhibitor; **R-ISS**, Revised International Staging System; **RRMM**, relapsed/refractory multiple myeloma.

References: 1. Hassan H and Szalat R. Appl Clin Genet 2021;14:241–54; 2. Hanumura I, et al. Int J Hematol 2022; 115:762–777; 3. Schmidt TM, et al. Blood Cancer J 2021;11:83; 4. Hanamura I. Cancers 2021;13:256; 5. Bisht K, et al. Exp Rev Haem 2021;14:1099–114; 6. Garcia J, et al. Cells 2021;10:1360; 7. Golay J and Taylor R. Antibodies 2020;9:58; 8. Harrison SJ, et al. Br J Haematol 2021;194:120–31; 9. Hanamura I, et al. Blood 2006;108:1724–32; 10. D'Agostino M, et al. Presented at IMW 2021. Abstract 1062754; 11. Costa LJ et al. Presented at ASH 2021. Abstract 481 (oral presentation); 12. Weinhold N, et al. Haematologica 2021;106:2754–8; 13. Abdallah N, et al. Blood Cancer J 2022;12:21; 14. D'Agostino M, et al. Presented at ASH 2020. Abstract 1329; 15. Sonneveld P, et al. Blood 2016;127:2955–62; 16. Dimopoulos MA, et al. Ann Oncol 2021;32:309–22; 17. mSMART treatment of Newly Diagnosed Myeloma **https://www.msmart.org/mm-treatment-guidelines**.

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