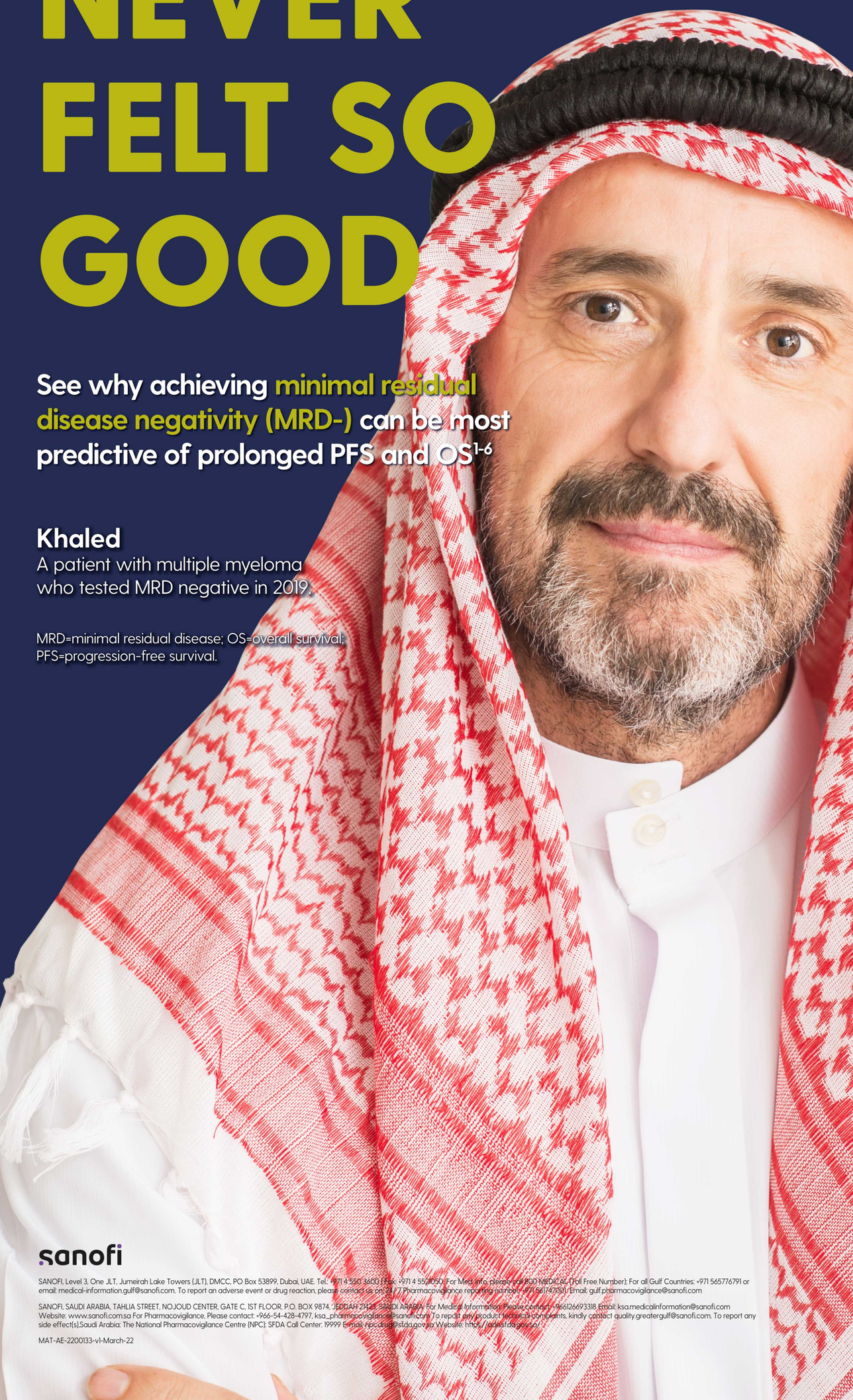
In multiple myeloma,

NEGATIVE NEVER FELT SO GOOD



See why achieving minimal residual disease negativity (MRD-) can be most predictive of prolonged PFS and OS[1-6]

Khaled
A patient with multiple myeloma who tested MRD negative in 2019.

MRD=minimal residual disease; OS=overall survival; PFS=progression-free survival.

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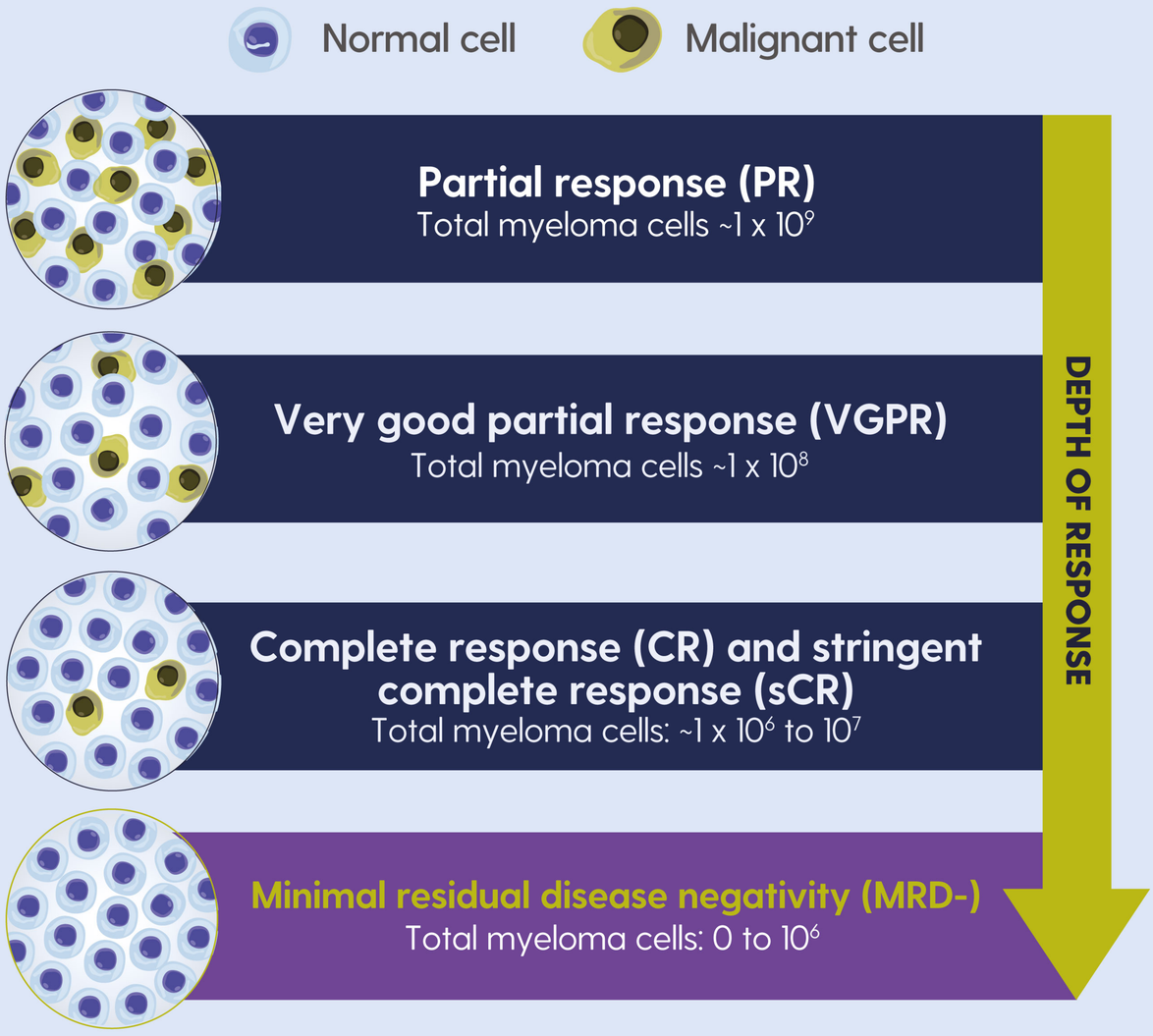
TO MAXIMISE LONG-TERM EFFICACY, ACHIEVING A DEEP RESPONSE IS IMPERATIVE[1]

MRD- is the deepest level of treatment response in multiple myeloma[7,8]

As advances in treatment have led to deeper responses, increasingly sensitive techniques are needed to evaluate the persistence of malignant cells after therapy. [1,2,9]

LEVEL OF TUMOUR BURDEN[7,10*]



- A patient who is MRD negative has an undetectable level of malignant cells in the bone marrow at a minimum sensitivity of 10^{-5} [7]
- Although some myeloma cells may remain, the number of malignant cells is below the threshold of detection of currently available tests[3,7]

*While standard response categories (PR, VGPR, and CR as noted in IMWG response criteria) are determined by measuring M-protein or free light chain levels in urine and blood samples, MRD status is determined by a direct measure of malignant cells in the bone marrow. IMWG criteria do not include tumour cell count when defi ning PR, VPGR, and CR.

CR=complete response; IMWG=International Myeloma Working Group; mPFS=median progression-free survival; MRD=minimal residual disease; MRD-=minimal residual disease negative/negativity; MRD+=minimal residual disease positive/positivity; NDMM=newly diag-nosed multiple myeloma; OS=overall survival; PFS=progression-free survival.

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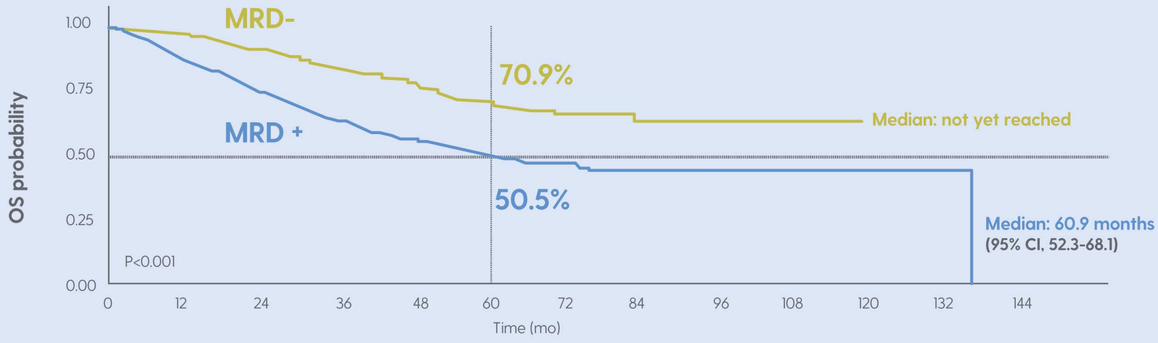
ACHIEVING MRD NEGATIVITY IS THE MOST POWERFUL INDICATOR OF PROLONGED PFS AND OS[1-6]

MRD- is associated with signifi cantly improved survival[3]

5-year OS in newly diagnosed transplant-eligible patients (N=2,250)[a]



Adapted from Munshi NC et al. *Blood Adv*. 2020.

MRD- is consistently associated with improved PFS and OS regardless of disease setting, method of MRD assessment, or sensitivity threshold.[3]

Even among patients who achieve CR, remaining MRD+ is associated with poorer prognosis[4]

Patients in CR with persistent MRD (MRD+)

27 MONTHS mPFS[b]

VS

Patients in CR with undetectable MRD (MRD-)

63 MONTHS mPFS[b]

Looking to treatments that achieve high rates of MRD negativity for patients is increasingly important to ensure better outcomes[1,11]

[a]Findings based on a large meta-analysis of 15 studies that reported OS rates in patients with transplant-eligible NDMM (N=2,250).[3]
[b]Findings based on a pooled analysis of 3 clinical trials that evaluated patients with transplant-eligible and -ineligible NDMM (N=609).[4]

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NEGATIVE NEVER FELT SO GOOD

Khalid
A patient with multiple myeloma
who tested MRD negative in 2019.

Treatments demonstrating high rates of MRD negativity can give more patients a chance for improved long-term outcomes[1,11]

REFERENCES: 1. Kostopoulos IV, Ntanasis-Stathopoulos I, Gavriatopoulou M, Tsitsilonis OE, Terpos E. Minimal residual disease in multiple myeloma: current landscape and future applications with immunotherapeutic approaches. *Front Oncol*. 2020;10:860. **2.** Dimopoulos MA, Moreau P, Terpos E, et al. Multiple myeloma: EHA-ESMO Clinical Practice Guide-lines for diagnosis, treatment and follow-up. *Ann Oncol*. 2021;32(3):309-322. **3.** Munshi NC, Avet-Loiseau H, Anderson KC, et al. A large meta-analysis establishes the role of MRD negativity in long-term survival outcomes in patients with multiple myeloma. *Blood Adv*. 2020;4(23):5988-5999. **4.** Lahuerta J-J, Paiva B, Vidriales M-B, et al. Depth of response in multiple myeloma: a pooled analysis of three PETHEMA/GEM clinical trials. *J Clin Oncol*. 2017;35(25):2900-2910. **5.** Martinez-Lopez J, Wong SW, Shah N, et al. Clinical value of measurable residual disease testing for assessing depth, duration, and direction of response in multiple myeloma. *Blood Adv*. 2020;4(14):3295-3301. **6.**Goicoechea I, Puig N, Cedena M-T, et al. Deep MRD profiling defines outcome and unveils different modes oftreatment resistance in standard- and high-risk myeloma. *Blood*. 2021;137(1):49-60. **7.** Kumar S, Paiva B, Anderson KC, etal. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment inmultiple myeloma. *Lancet Oncol*. 2016;17(8):e328-e346. **8.** Burgos L, Puig N, Cedena M-T, et al. Measurableresidual disease in multiple myeloma: ready for clinical practice? *J Hematol Oncol*. 2020;13(1):82. **9.** Avet-Loiseau H,Ludwig H, Landgren O, et al. Minimal residual disease status as a surrogate endpoint for progression-free survival innewly diagnosed multiple myeloma studies: a meta-analysis. *Clin Lymphoma Myeloma Leuk*. 2020;20(1):e30-e37. **10.**Paiva B, van Dongen JJM, Orfao A. New criteria for response assessment: role of minimal residual disease inmultiple myeloma. *Blood*. 2015;125(20):3059-3068. **11.** Landgren O, Iskander K. Modern multiple myeloma therapy: deep,sustained treatment response and good clinical outcomes. *J Intern Med*. 2017;281(4):365-382.

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