MultipleMyelomaHub

Patients non-eligible for transplant

FDA approves triplet of D-Rd for patients with NDMM who are not eligible for ASCT

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The United States (US) Food & Drug Administration (FDA) has approved the use of daratumumab (D), lenalidomide (R) and dexamethasone (d; D-Rd) in patients with newly diagnosed multiple myeloma (NDMM) who are not eligible for autologous stem cell transplant (ASCT).[1-3]

The approval is based on the results of the phase III MAIA study (MMY 3008) which compared D-Rd to Rd alone. The interim results of the study were presented by Thierry Facon during the late breaking abstracts session at the 60th American Society of Hematology (ASH) meeting in San Diego, CA, in December 2018.[4]

Whilst this brings a new option to patients with non-transplant eligible NDMM in the US, this regimen is not yet approved in Europe, though a type II variation application was previously submitted to the European Medicines Agency (EMA).[5]

MAIA trial results[4,5]

The phase III MAIA trial compared D-Rd (n = 368) to Rd alone (n = 369) in patients with NDMM who were not candidates for ASCT. The primary endpoint of the study was progression-free survival (PFS).

At a median follow-up of 28 months, the PFS rate for the D-Rd arm was not reached (NR), compared to 31.9 months for the Rd arm. The D-Rd regimen gave a 44% reduction in the risk of progression or death with a higher rate of minimal residual disease (MRD) negativity (10^{-5}) which was 24% with D-Rd arm *versus* 7% with Rd ($P < 0.0001$). **Table 1** shows a further breakdown of results.

Overall, the D-Rd triplet led to deeper responses, a three-fold higher MRD negativity rate, and had a comparable safety profile to that reported in other studies such as POLLUX and ALYCONE.

Table 1: Summary of MAIA clinical trial[4,5]

Trial name	MAIA (MMY3008)
NCT reference	NCT02252172

Drug combination	DRd (daratumumab, lenalidomide, dexamethasone) Rd (lenalidomide, dexamethasone)
Patient setting	Transplant ineligible NDMM
Trial phase	Phase III
Trial design	DRd *versus* Rd
N	737
Dosing schedule	Rd: oral lenalidomide (25 mg) on days 1–21 of a 28-day cycle with 40 mg dexamethasone once per week. DRd: As per Rd arm with the addition of intravenous daratumumab (16 mg/kg) once weekly for cycles 1–2, every 2 weeks for cycles 3–6 and every 4 weeks for cycle 7 onwards until disease progression, unacceptable toxicity or study end
Primary endpoint	Progression-free survival (PFS)
Efficacy *(Given as DRd vs Rd)*	Median follow-up: 28 months Median PFS: not reached *vs* 31.9 months ≥Complete response (CR): 47.6% *vs* 24.7% Overall response rate (ORR): 93% *vs* 81% Risk of reduction of disease progression or death with DRd *vs* Rd alone: 44% (HR 0.56, 95% CI, 0.43–0.73, $P < 0.0001$)
Safety	In the DRd arm, there were higher rates (≥5% difference) of grade 3/4 pneumonia, neutropenia and leukopenia Safety profile is in line with previously reported daratumumab studies

Read the full results reported during the ASH 2018 meeting here.

References

1. Upfront Daratumumab/Rd Combo Approved by FDA for Transplant-Ineligible Myeloma https://www.targetedonc.com/news/upfront-daratumumabrd-combo-approved-by-fda-for-transplantineligible-myeloma [accessed 2019 Jun 28]
2. Daratumumab prescribing information (FDA). https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761036s020lbl.pdf
3. Drugs@FDA: FDA Approved Drug Products. Daratumumab (BLA 761036) https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process [accessed 2019 Jun 28]
4. Facon T. *et al*. Phase 3 Randomized Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patients with Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant (MAIA). 2018 Dec 4; LBA #2: ASH 60th Annual Meeting and Exposition, San Diego, CA.
5. EU Approval Sought for Frontline Daratumumab/Rd in Transplant-Ineligible Myeloma https://www.onclive.com/web-exclusives/eu-approval-sought-for-frontline-daratumumabrd-in-transplantineligible-myeloma [accessed 2019 March 28]