Darzalex® (daratumumab), Kyprolis® (carfilzomib) – Expanded indication

- On August 20, 2020, the FDA approved the combination use of Janssen's Darzalex (daratumumab) with Amgen's Kyprolis (carfilzomib) and dexamethasone in adult patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy.

    - Previously, Darzalex had been approved for adults with multiple myeloma as monotherapy or in combination with other agents (but not with Kyprolis).
    - Previously, Kyprolis had been approved for adults with relapsed or refractory multiple myeloma who have received one to three lines of therapy in combination with lenalidomide/dexamethasone, or with dexamethasone.

- Efficacy was demonstrated in two trials: CANDOR evaluated a combination with twice-weekly Kyprolis/Dexamethasone and EQUULEUS evaluated combination with once weekly Kyprolis/Dexamethasone.

- CANDOR was a randomized, open-label, multicenter clinical trial in patients with relapsed or refractory multiple myeloma who had failed at least one to three prior lines of therapy.

    - A total of 466 patients were randomized to receive Darzalex + Kyprolis (twice weekly) + Dexamethasone (n = 312) or Kyprolis + Dexamethasone (n = 154).
    - The median age was 64 years (range 29 to 84 years). Patients had received a median of 2 prior lines of therapy and 58% of patients had received prior autologous stem cell transplantation (ASCT). The majority of patients (92%) received a prior proteosome inhibitor (PI) and of those 34% were refractory to PI including regimen. Fourty-two percent (42%) of patients had received prior lenalidomide and of those, 33% were refractory to a lenalidomide containing regimen.
    - Efficacy was evaluated by an independent review committee evaluation of progression-free survival (PFS) using standard response criteria from the International Myeloma Working Group (IMWG). The median PFS had not yet been reached in the triple combination arm and was 15.8 months in the Kyprolis + dexamethasone arm (hazard ratio = 0.63; 95% CI: 0.46, 0.85; p = 0.0014).

- EQUULEUS was an open-label, multi-cohort trial, in patients with relapsed or refractory multiple myeloma who had failed at least one to three prior lines of therapy.
    - A total of 85 patients were enrolled and all received Darzalex + Kyprolis (once weekly) + Dexamethasone.
    - The median patient age was 66 years (range: 38 to 85 years) with 9% of patients were 75 years of age or older. Patients had received a median of 2 prior lines of therapy. Seventy-three percent (73%) of patients had received prior ASCT. All patients received prior bortezomib, and 95% of patients received prior lenalidomide. Fifty-nine percent (59%) of patients were refractory to lenalidomide and 29% of patients were refractory to both a PI and thalidomide or thalidomide analogue.
    - Efficacy was based on overall response rate using IMWG criteria. The overall response rate was 81% (95% CI, 71, 89). The median time to response was 0.95 months (range: 0.9, 14.3). The median duration of response was 28 months (95% CI: 20.5, not estimable).

- The recommended dose of Darzalex is 16mg/kg based on actual body weight. See full prescribing information for details on combination and schedule.

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- The recommended dose of Kyprolis is 56 mg/m^2 or 70 mg/m^2 based on body surface area. See full prescribing information for details on combination and schedule.

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