S176 DARATUMUMAB CARFILZOMIB LENALIDOMIDE AND DEXAMETHASONE AS INDUCTION THERAPY IN HIGH-RISK TRANSPLANT ELIGIBLE NEWLY DIAGNOSED MYELOMA PATIENTS: RESULTS OF THE PHASE 2 STUDY IFM 2018-04

Author(s):
Cyrille Touzeau, Aurore Perrrot, Cyrille Hulin, Salomon Manier, Margaret Macro, Marie-Lorraine Chretien, Lionel Karlin, Olivier Decaux, Caroline Jacquet, Mourad Tiab, Xavier Leleu, Lucie Planchce, Hervé Avet-Loiseau, Philippe Moreau

EHA Library. Touzeau C. 06/10/22; 357040; S176

Background:
High-risk (HR) cytogenetic is associated with poor outcome in transplant eligible (TE) newly diagnosed myeloma multiple myeloma (NDMM). The triplet combination carfilzomib lenalidomide and dexamethasone (KRD) plus transplantation demonstrated high efficacy with favorable safety profile in TE-NDMM patients (FORTE). The addition of daratumumab (Dara) to frontline therapy also improved response rate and progression free-survival in TE-NDMM patients (CASSIOPEIA, GRIFFIN). Double transplant also improved outcome of HR TE NDMM patients (EMN02, STAMINA).

Aims:
The phase 2 trial 2018-04 from the Intergroupe Francophone du Myelome (IFM) is evaluating an intensive strategy with Dara-KRD induction and consolidation plus double transplant in HR TE NDMM (NCT03606577).

Methods:
HR MM was defined by the presence of del17p, t(4;14) and/or t(14;16). Stategy includes Dara-KRD induction (6 cycles), autologous stem cell transplantation (ASCT), Dara-KRD consolidation (4 cycles), second ASCT, Dara-lenalidomide maintenance. The primary endpoint was the feasibility of this intensive strategy. Here, we report efficacy and safety analysis of Dara-KRD induction.

Results:
Fifty patients with previously untreated NDMM were included from july 2019 to march 2021 in 11 IFM centers Median age was 57 (range 38 -65). ISS stage 3 was present in 12 (24%)

patients. Based on inclusion criteria, all patients had HR cytogenetic, including 17p deletion (n=20, 40%), t(4;14) (n=26, 52%) or t(14;16) (n=10,20%). Forty-six patients completed Dara-KRD induction. Two patients discontinued treatment due to severe adverse event (COVID-19 infection, n=1 ; drug-induced hepatitis, n=1) and 2 patients discontinued treatment due to disease progression. Grade 3-4 treatment related adverse event (>5% of patients) were neutropenia (38%), anemia (14%), thrombocytopenia (8%), infection (6%), renal insufficiency (6%) and deep-vein thrombosis (6%). Two patients (6%) experienced stem-cell collection failure. Overall response rate was 96%, including 92 % > very good partial response. Among 37/46 evaluable patients post induction, Minimal Residual Disease negativity rate (NGS, 10-5) was 62%.

Conclusion:

Dara-KRD as induction prior ASCT is safe and allows deep responses in TE NDMM patients with high-risk cytogenetic profile. IFM 2018-04 study is ongoing and longer follow-up is needed to evaluate safety and efficacy of the overall strategy with Dara-KRD induction and consolidation plus double transplant in this subset of HR patients.

Keyword(s):

Autologous stem cell collection, High risk, Myeloma