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ORAL ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

Daratumumab, Carfilzomib, Lenalidomide, and Dexamethasone Induction and Consolidation with Tandem Transplant in High-Risk Newly Diagnosed Myeloma Patients: Final Results of the Phase 2 Study IFM 2018-04

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Background: High-risk (HR) cytogenetic is associated with poor outcome in transplant eligible (TE) newly diagnosed 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). The phase 2 trial 2018-04 from the Intergroupe Francophone du Myelome (IFM) evaluated 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). Treatment strategy included Dara-KRD induction (6 cycles), autologous stem cell transplantation (ASCT), Dara-KRD consolidation (4 cycles), second ASCT, Dara-lenalidomide maintenance for 2 years. The primary endpoint was the feasibility of this intensive strategy.
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). 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%). Four (8%) patients had extramedullary disease. At data cut-off, the study met the primary endpoint with 36 (72%) patients completing second transplant. Twenty-one patients (42%) discontinued the study, due to stem-cell collection failure (n=8), disease progression (n=8), adverse event (n=4), consent withdrawal (n=1). Grade 3-4 Dara-KRD induction/consolidation related adverse event (>5% of patients) were neutropenia (44%), anemia (22%), thrombocytopenia (24%) and infection (14%). Four patients discontinued treatment due to severe adverse event (COVID-19 infection, drug-induced hepatitis, JC virus related encephalopathy, intracerebral hemorrhage). Seven patients died, 5 due to disease progression and 2 due to infection. Responses deepened over time with an overall response rate before maintenance of 100%, including 81 % complete response. Among evaluable patients (33/36), pre maintenance Minimal Residual Disease negativity rate (NGS, 10 $^{-6}$) was 94%. After a median follow up of 32 months, the 24-months PFS is 87% (78-87%) and the 24-months OS is 94% (87-100%).

Conclusions: Dara-KRD induction/consolidation with tandem transplant was feasible in TE NDMM patients with high-risk cytogenetic profile, and resulted in high MRD negativity rate and high progression free survival.

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