Phase 3 randomized study of daratumumab (DARA) + bortezomib/thalidomide/dexamethasone (D-VTd) vs VTd in transplant-eligible (TE) newly diagnosed multiple myeloma (NDMM): CASSIOPEIA Part 1 results.

Presented Sunday, June 2, 2019

Authors:
Philippe Moreau, Michel Attal, Cyrille Hulin, Marie-Christine Béné, Annemiek Broijl, Denis Caillot, Michel Delforge, Thomas Dejoie, Thierry Facon, Jérôme Lambert, Xavier Leleu, Margaret Macro, Aurore Perrot, Sonja Zweegman, Tahamtan Ahmadi, Christopher Chiu, Lixia Pei, Jessica Vermeulen, Herve Av[illegible] Print Loiseau, Pieter Sonneveld, on behalf of IFM and HOVON; Hematology, University Hospital Hôtel-Dieu, Nantes, France; Institut Universitaire du Cancer de Toulouse-Oncopole, Toulouse, France; Department of Hematology, Hospital Haut Leveque, University Hospital Bordeaux, Pessac, France; Hematology Biology, University Hospital Hôtel Dieu, Nantes, France; Erasmus MC Cancer Institute, Rotterdam, Netherlands; CHU Dijon, Hôpital Du Bocage, Dijon, France; Universitaire Ziekenhuizen Leuven, Leuven, Belgium; Biochemistry Laboratory, Hospital of Nantes, Nantes, France; Service des Maladies du Sang, Hôpital Claude Huriez, Lille, France; Biostatistical Department, Hôpital Saint Louis, Paris, France; CHU Poitiers-Hôpital la Milétrie, Poitiers, France; Centre Hospitalier Universitaire (CHU) de Caen, Caen, France; Department of Hematology, University Hospital, Vandoeuvre-Lès-Nancy, France; Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Hematology, Amsterdam, Netherlands; Genmab US, Inc., Princeton, NJ; Janssen Research & Development, Spring House, PA; Janssen Research & Development, Raritan, NJ; Janssen Research & Development, LLC, Leiden, Netherlands; Unite de Genomique du Myelome, IUC-T Oncopole, Toulouse, France

View Less

Abstract Disclosures

Background:
VTd is a standard of care (SoC) for TE NDMM. CD38 mAb DARA significantly reduced the risk of progression/death and improved CR and MRD-negative rates in relapsed refractory MM or transplant-ineligible NDMM in phase 3 studies. We report the primary and final analysis of Part 1 of CASSIOPEIA.

Methods:
In Part 1, TE NDMM pts 18-65 y were randomized 1:1 to VTd (6 28-day cycles [C; 4 pre-ASCT induction, 2 post-ASCT consolidation] of V 1.3 mg/m^2 SC BIW Week [W] 1-2; T 100 mg PO QD; d 40-80 mg/week

PO or IV W 1-4 C 1-2, W 1-3 C 3-6) ± DARA (16 mg/kg IV QW C 1-2, Q2W C 3-6). Melphalan 200 mg/m^2 was pre-ASCT HDT. The primary endpoint, post-consolidation sCR rate, was assessed at Day [D] 100 post-ASCT. Part 2 (maintenance) is ongoing.

Results:

A cohort of 1085 pts (D-VTd, 543; VTd, 542) was randomized. The D 100 post-ASCT sCR rate was significantly higher for D-VTd vs VTd (28.9% vs 20.3%; *P* = 0.0010; Table). At 18.8-mo median follow-up, PFS from first randomization favored D-VTd with HR 0.47 (95% CI, 0.33-0.67; *P*<0.0001). With median PFS NR in either arm, 18-mo PFS rates were 92.7% vs 84.6% for D-VTd vs VTd. Rates of ≥CR, ≥VGPR, and MRD negativity supported sCR results (Table). OS is immature with 46 deaths on study (D-VTd, 14; VTd, 32; HR, 0.43; 95% CI, 0.23-0.80). The most common (≥10%) grade 3/4 TEAEs (D-VTd/VTd) were neutropenia (27.6%/14.7%), lymphopenia (17.0%/9.7%), stomatitis (12.7%/16.4%), and thrombocytopenia (11.0%/7.4%). In the D-VTd arm, infusion-related reactions occurred in 35.4% of pts.

Conclusions:

D-VTd in induction prior to and consolidation after ASCT improved depth of response (sCR, ≥CR, and MRD negativity) and PFS with acceptable safety. The favorable benefit-risk profile supports the use of D-VTd in TE NDMM. CASSIOPEIA is the first study to demonstrate clinical benefit of DARA + So Print NDMM. Clinical trial information: NCT02541383

Post-consolidation (D 100 Post-ASCT) Response and MRD-negative Rates: ITT.

	D-VTd, %	VTd, %	OR (95% CI)	*P*
sCR	28.9	20.3	1.60 (1.21-2.12)	0.0010
≥CR	38.9	26.0	1.82 (1.40-2.36)	<0.0001
≥VGPR	83.4	78.0	1.41 (1.04-1.92)	0.0239
MRD-negative (10^{-5})	63.7	43.5	2.27 (1.78-2.90)	<0.0001
≥CR + MRD-negative (10^{-5})	33.7	19.9	2.06 (1.56-2.72)	<0.0001