Subcutaneous Daratumumab (DARA) in Patients (Pts) With Relapsed or Refractory Multiple Myeloma (RRMM): Part 2 Update of the Open-label, Multicenter, Dose-escalation Phase 1b Study (PAVO)

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INTRODUCTION

Daratumumab is a human IgGκ monoclonal antibody to the cell surface CD38 molecule, which is expressed in malignant plasma cells of patients with RRMM. The antibody is conjugated to a truncated form of PEGylated hyaluronidase (rHuPH20), which cleaves the hyaluronan barrier in the extracellular matrix to facilitate subcutaneous (SC) administration.

METHODS

A Phase I/II dose-escalation study (NCT02519452) was conducted to evaluate tolerability, pharmacokinetics, pharmacodynamics, and clinical activity of single-agent DARA IV and SC regimens in RRMM. Pts were scheduled to receive either (1) 1,800 mg DARA SC weekly, (2) 1,800 mg DARA SC every 2 weeks (Q2W), or (3) 1,800 mg every 4 weeks (Q4W). DARA QW in Cycles 1 and 2, Q2W in Cycles 3 through 6, and Q4W thereafter. A total of 4 cycles were planned with a maximum of 28 doses. An adaptive escalation scheme was used.

RESULTS

PAVÖ study design

Pharmacokinetics

Daratumumab concentration profiles are displayed in Table 1. The SC route was associated with delayed absorption of daratumumab, with a median time to peak of 7 days. A moderate accumulation of daratumumab was observed after SC dosing, with a steady-state volume of distribution of 2,000 L.

Safety

The incidence and severity of IRRs was low with DARA SC. The most common TEAEs were injection site reactions (50%), pyrexia (24%), and chills (16%). The incidence of SAEs was low (16%). There were no DARA SC-related deaths.

CONCLUSIONS

DARA SC 1,800 mg was well tolerated, with a moderate accumulation of daratumumab and a good tolerability profile. The incidence of IRRs was low with DARA SC. Two DARA SC regimens (1,800 mg Q2W and Q4W) were supported for further evaluation in the Phase 2/3 PAVÖ 2 study. PAVÖ 2 will evaluate additional dose levels of DARA SC to establish the optimal regimen and will provide data on clinical activity and safety.

REFERENCE

1. Chari JJD63623. Presented at: Annual Meeting of the American Society of Clinical Oncology (ASCO); June 1-5, 2018; Chicago, Illinois.

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